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(54) Title: PERIPHERAL BLOOD CELL MARKERS USEFUL FOR DIAGNOSING MULTIPLE SCLEROSIS AND METHODS AND KITS UTILIZING SAME

(57) Abstract: Markers of multiple sclerosis and methods and kits utilizing same for diagnosing multiple sclerosis in an individual are provided.

PERIPHERAL BLOOD CELL MARKERS USEFUL FOR DIAGNOSING MULTIPLE SCLEROSIS AND METHODS AND KITS UTILIZING SAME

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates generally to the field of diagnosis, treatment assessment and prognosis. More specifically, the present invention relates to peripheral blood cell expressed markers and kits and methods utilizing same for diagnosing, treating and assessing the state of multiple sclerosis (MS) in an individual. The present invention also provides cellular markers which are useful in distinguishing between different clinical courses of MS e.g.: probable, relapsing-remitting, secondary progressive or primary progressive as well as response to the therapy.

Multiple sclerosis is an autoimmune neurodegenerative disease, which is marked by inflammation within the central nervous system with lymphocyte attack against myelin produced by oligodendrocytes, plaque formation and demyelization with destruction of the myelin sheath of axons in the brain and spinal cord, leading to significant neurological disability over time. The disease frequently occurs in young adults between 20-40 years of age, is more prevalent in females than males (2:1), and has a characteristic geographical distribution – estimated prevalence in USA 120/100,000, (250,000 to 350,000 cases).

The annual cost of MS in USA was estimated about $34,000 per person, $2.2 million total lifetime cost per case or $6.8 billion yearly, in a conservative estimate of a national annual cost (Anderson DW, 1992; Whetten-Goldstain K., 1998).

Clinical Diagnosis and Evaluation of Stages of MS

Typically, at onset an otherwise healthy person presents with the acute or sub acute onset of neurological symptomatology (attack) manifested by unilateral loss of vision, vertigo, ataxia, dyscoordination, gait difficulties, sensory impairment characterized by paresthesia, dysesthesia, sensory loss,

urinary disturbances until incontinence, diplopia, dysarthria or various degrees of motor weakness until paralysis. The symptoms are usually painless, remain for several days to a few weeks, and then partially or completely resolve. After a period of remission, a second attack will occur. During this period after the first attack, the patient is defined to suffer from probable MS. Probable MS patients may remain undiagnosed for years. When the second attack occurs the diagnosis of clinically definite MS (CDMS) is made (Poser criteria 1983; C.M. Poser et al., Ann. Neurol. 1983;13, 227).

The clinical disease courses of MS are relapsing-remitting, primary or secondary progressive (Abramsky, 1997; Russell, 1998).

The relapsing-remitting course of MS (85% of patients) is characterized by acute attacks or relapses during which new neurological symptoms and signs appear, or worsen. Relapse develops within a period of several days, lasts for 6-8 weeks, than gradually resolves. During the acute relapse scattered inflammatory and demyelinating central nervous system (CNS) lesions produce varying combinations of motor, sensory, coordination, visual, and cognitive impairments, as well as symptoms of fatigue and urinary tract dysfunction. The outcome of a relapse is unpredictable in terms of neurological sequel but it is well established that with additional relapses, the probability of complete clinical remission decreases and neurological disability and handicap may develop. On average, about 60% of patients remain fully functional 10 years after the primary attack, and 25 to 30% remain fully functional 30 years after onset. Statistically, the disease does not greatly decrease life expectancy (mean decrease 12 years), although some patients become severely disabled and die from recurrent infections and complications.

Primary progressive MS (10% of patients) is characterized by slow, progressive neurological dysfunction usually in the form of a gradual myelopathy causing spasticity and ataxia. Treatment regimen varies greatly with different clinical course and severity of the disease.

The diagnosis of MS is still defined primary by clinical terms and relies on a combination of history, neurological examination and ancillary laboratory and neuro-imaging studies.

Laboratory tests for MS include: 1) CSF evaluation of IgG synthesis, oligoclonal bands; 2) MRI of the brain and spinal cord and; 3) exclusion of other autoimmune diseases by blood tests [e.g.,; serum B12 level; HTLV 1 or HIV 1 titers; sedimentation rate or C-reactive protein; RA latex (Rheumatoid arthritis); ANA, anti-DNA antibodies (systemic lupus erythematosus)]. However, accurate diagnosis and prognosis in the "probable" stage, and early relapsing-remitting stages remains problematic. For example, it has been shown that positive MRI findings in the first demyelinating attack only provide a 50% successful prediction of development of clinically definite MS within 2-3 years (CHAMPS Study Group, Neurology 2002;59:998-1005). Likewise, Villar et al (Neurology 2002;59:877-83) found that detection of oligoclonal IgM bands with early symptoms were only partially predictive of development of clinically definite MS.

Other laboratory tests may provide some additional support for the diagnosis, but evidence of lesions disseminated in time and space remains a cardinal element of the diagnosis (Poser CM., 2001). In absence of definitive laboratory tests and pathognomonic clinical features, MS remains ultimately a diagnosis of exclusion.

Diseases that may be confused with MS are: 1) Acute disseminated encephalomyelitis (follows infections or vaccination mainly in children, fever, headaches, and meningitis common), 2) Lyme disease (antibodies to Borrelia species antigens in serum and CSF), 3) HIV associated myelopathy (HIV antibodies present), 4) HTLVI myelopathy (HTLVI antibodies present in serum/CSF), 5) Neurosyphilis (syphilis antibodies present in serum and/or CSF, 6) Progressive multifocal leukoencephalopathy (biopsy of lesions demonstrates virus by electron microscopy), 7) Systemic lupus erythematosus (CNS manifestations of lupus, antinuclear antibodies, anti-dsDNA), 8) Polyarteritis

nodosa (systemic signs, micro-aneurysms demonstrated by angiographies, vasculitis demonstrated in biopsy of involved areas), 9) Sjogren's syndrome (dry eyes and mouth, antiRo and antiLa antibodies), 10) Behcet's disease (Oral/genital ulcers, antibodies to oral mucosa), 11) Sarcoidosis (CNS signs, increased protein in CSF, biopsy shows granuloma, 12) Paraneoplastic syndromes (older age group, antiYo antibodies), 13) Subacute combined degeneration of cord (peripheral neuropathy, vitamin B12 levels), 14) Sub acute myeloopticoneuropathy (adverse reaction to chlorhydroxyquinoline, mainly in Japanese), 15) Hereditary spastic paraparesis/ primary lateral sclerosis (normal CSF, MRI and visual evoked potential studies), 16) Adrenomyeloneuropathy (adrenal dysfunction, neuropathy, increased plasma very long-chain fatty acids), 16) Spinocerebellar syndromes (familial, pes cavus scoliosis, abnormal reflexes, normal CSF IgG), 17) Miscellaneous – strokes, tumors, arteriovenous malformations, arachnoid cysts, Arnold-Chiari malformations, and cervical spondylosis all may lead to diagnostic dilemmas on occasion. Thus, detailed history and neurological examination must be complemented by specific laboratory tests for the correct diagnosis of MS. Clearly there is a long felt need for more powerful diagnostic tools for prediction and staging of MS.

Etiology of MS

The etiology of MS is unknown. It is suggested that a combination of genetic background and environmental factors and immune response are involved in the disease. A certain incidence of familial occurrence has been observed, with the concordance rate among monozygotic twins being 30%, a 10-fold increase over that in dizygotic twins or first-degree relatives (Steinman, 1966; Dyment et al Mol. Gen 1997;6:1693-98). In addition, recent research indicates that the tissue damage in MS occurs as the result of pathological autoimmune responses to several myelin antigens following exposure to an as yet undefined environmental causal agent.

However, although some environmental factors have been statistically associated with the disease, none have provided correlations of any predictive

value. Environmental factors seem to trigger MS in subjects who are already genetically susceptible to the illness. Most probably no one dominant gene determines genetic susceptibility, but rather many genes, each with different influence, are involved. Indeed, the initial pathogenic process could be caused by one group of genes, while others groups could be responsible for the development and progression of the disease (Oksenberg, 2001; Compston, 1997).

Microarray Analysis and MS

Microarray technology is based on hybridization of mRNA to high-density array of immobilized target sequences. Each sequence corresponds to a specific gene(s) of interest. The labeled pool of sample mRNA is subsequently hybridized to the array (chip). Application of this technology provides the capability of monitoring thousands of various genes simultaneously. Today commercial available DNA microarrays (Affymetrix, Santa Clara CA, USA) contain elements representing 10,000, 20,000 or more genes that have been characterized in terms of function or disease association. The preparation and use of microarrays for diagnostics, research and drug development is disclosed in, inter alia, US Pat. Nos. 6,324,497 and 6,468,476 to Friend et al and 6,410,229 to Lockhart et al; and Intnl Pat. Application WO 0053625C2 and A2.

Several application of microarrays in human disease have been reported, for example the identification (marker) genes involved in ovarian carcinogenesis (Ono K., 2000); classification of genes expression profiling of cutaneous malignant melanoma (Bitter M., 2000); and expression profile of Tangl-Rearing CA1 neurons in Alzheimer's disease (Stephen, 2000). Alizaden (2000) characterized gene expression in diffuse large B cell lymphoma, where two distinct gene expression patterns, characterized by different molecular forms of B cells lymphoma, were identified. In addition, microarray technology has also been applied to diagnosis and monitoring of such diverse diseases as cancer (US Pat. No. 6,511,849 to Freuhauf et al), psoriasis (Intnl Pat. Application WO 20020027538 to Trepicchio et al), T-helper cell related

diseases (Trepicchio et al , Intnl Pat Application WO 20020039734), Epstein-Barr disease (U.S. Pat. Nos. 6,506,553 and 6,468,476 to Smith and Parks), rheumatoid arthritis (Intnl Pat Application WO 0248310A2 to Trepicchio et al) and Reward Deficiency Syndrome, all of which are incorporated herein by reference.

In a recent review (Greenberg SA., 2001) the author discussed the potential application of DNA microarray technology for understanding neurological disorders. Using cDNA microarrays technology, brain tissue from pathology lesions and normal white matter of single MS patient were analyzed (Whitney LW.,1999). Blood genomic fingerprints were demonstrated after experimental strokes, seizures, hypoglycemia and hypoxia of rats (Yang Tang, 2001). Similarly, microarray analysis of gene expression in brainstem and spinal cord tissues from the animal models of MS (experimental autoimmune encephalomyelitis, EAE) has identified a number of differentially expressed genes from active-acute versus silent lesions (Lock C. et al Nat Med 2002;8,500-504), and also suggested a role for the proinflammatory cytokine osteopontin in the development of EAE in mice (Chabas D et al Science 2001;294:1731-34).

In another recent study, Ramanathan M et al (J of Immunology 2001;116:213-19) used cDNA microarray technology to identify abnormal gene expression patterns in PBMC of relapsing-remitting MS patients. The study compared PBMC gene expression in 15 patients during remission (only) with that of 15 healthy controls, using a GeneFilters GF211 array (Research Genetics, Huntsville AL, USA) having approximately 5200 human gene sequences. Groups of marker genes correlated with MS were disclosed, but the range of differences (fold changes) between level of gene expression in MS and control groups was only 13 to 35 % for unregulated and from 11 to 43% for down regulated genes. Such small differences are probably due to the limited sensitivity of the technology employed in using GeneFilters arrays, and may not have any clinical or diagnostically mining significance. More significantly, the

population of MS patients was limited, including only patients during clinical remission, who had not received any immunosupressive treatment for at least 3 months. Thus, the markers described do not provide a profile of expression patterns useful for diagnosing clinically defined MS in patients having probable MS, or for determining stages of the disease.

Trepicchio et al. (Intnl Pat. Application No. WO 02/079218 A1) also describe the use of microarray technology in determining characteristic gene expression in an animal model of MS (murine EAE) and in tissue samples from MS patients. The human samples were PBMC or brainstem tissue, collected from 60 patients manifesting a wide variety of symptoms, at different stages of MS including relapsing-remitting, primary and secondary progressive, and acute exacerbation. RNA probes prepared from these samples were hybridized to a human chip array containing approximately 14,000 gene sequences (MicroArray, Affymetrix, cat no. 510448, Santa Clara CA), and expression profiles compared with those of healthy controls. Determination of the panel of "MS-related" markers was based merely on fold change of greater than 2 fold (up- or downregulated), with a confidence level of $p<0.01$. No more stringent statistical criteria were applied. A "panel" of 300 differentially regulated genes was thus described in the PBMC samples, and another 100 in the brain lesion tissue. However, no classification of expression profiles characteristic to specific stages of the disease was provided, and the "class predictor model", as described, using "neighborhood analysis", was applied for attempted prediction of "MS-afflicted" or "non-diseased" samples only. Thus, the panel of markers described is not applicable to the diagnosis of stage of MS, in general, is unsuited for the prediction of clinically definite MS or probable MS patients, and is clearly non-predictive in monitoring response to treatment.

There is thus a widely recognized need for, and it would be highly advantageous to have gene expression profiles useful in distinguishing between different forms of MS e.g.: probable, relapsing-remitting, primary or secondary as well as response to the therapy, devoid of the above limitations.

SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a method of diagnosing a subject with multiple sclerosis, the method comprising determining a level of expression of at least one gene selected from the group consisting of the genes listed in Tables I-V in a sample obtained from the subject, wherein a substantial difference between the level of expression of the gene in the sample obtained from the subject and a normal expression level of the gene is an indication that the subject is afflicted with multiple sclerosis.

According to further features in preferred embodiments of the invention described below a method of monitoring a state of multiple sclerosis in a subject, the method comprising monitoring a level of expression of at least one gene selected from the group consisting of the genes listed in Tables I-V over a predetermined time period, wherein substantial difference between the levels of expression of the at least one gene over the predetermined time period indicates a change in a state of the multiple sclerosis in the subject.

According to further features in preferred embodiments of the invention described below monitoring the level of expression of at least one gene over the predetermined time period is effected by periodically obtaining a sample from the individual and determining the level of expression of the at least one gene in the sample.

According to still further features in the described preferred embodiments the at least one gene comprises at least 10, at least 50, at least 100, at least 250, at least 500, at least 750, at least 1000 or at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V.

According to another aspect of the present invention there is provided a method of diagnosing a subject with multiple sclerosis, the method comprising the step of determining a level of expression of each of the genes listed in Tables I-V in a sample obtained from the subject, wherein a substantial difference between expression levels of the genes in the sample obtained from

the subject and normal expression levels of the genes is an indication that the subject is afflicted with multiple sclerosis.

According to further features in preferred embodiments of the invention described below the normal expression level of the at least one gene or genes is determined by measuring the level of expression of the gene or genes in at least one control sample obtained from at least one healthy individual.

According to still further features in the described preferred embodiments the sample includes peripheral blood mononuclear cells.

According to yet further features in the described preferred embodiments the substantial difference is a difference statistically significant at a confidence level of p= 0.05 as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

According to further features in preferred embodiments of the invention described below the level of expression of the at least one gene or genes is determined by quantifying a level of a protein product thereof in the sample.

According to still further features in the described preferred embodiments quantifying a level of the protein is effected using a reagent which specifically binds with the protein.

According to yet further features in preferred embodiments of the invention described below the reagent comprises an antibody or fragments thereof.

According to further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table I.

According to still further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table II.

According to yet further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table III.

According to further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table IV.

According to still further features in the described preferred embodiments at least one gene or genes are selected from the genes listed in Table V.

According to yet further features in preferred embodiments of the invention described below the level of expression of the at least one gene or genes in the sample is determined by detecting the presence in the sample of a transcribed polynucleotide or portion thereof. The transcribed polynucleotide can be mRNA.

According to further features in preferred embodiments of the invention described below the transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with the transcribed polynucleotide or portion thereof.

According to still further features in the described preferred embodiments the sample from a subject is T cells, the at least one gene or genes are selected from the genes listed in Table IV and the normal expression of the gene or genes is T-cell expression.

According to an additional aspect of the present invention there is provided a method of assessing the efficacy of a treatment regimen on multiple sclerosis in a subject, the method comprising determining a level of expression of at least one gene or genes selected from the group consisting of the genes listed in Tables I-V in samples obtained from the subject prior to, and following exposure to the treatment regimen, wherein a substantial difference in the expression level of at least one gene or genes between the samples is an indication that the treatment regimen is efficacious in treating multiple sclerosis in the subject.

According to further features in preferred embodiments of the invention described below the treatment regimen is administering at least one test compound for inhibiting multiple sclerosis.

According to still further features in the described preferred embodiments the treatment regimen is an environmental condition.

According to yet further features in the described preferred embodiments the substantial difference is a difference statistically significant at a confidence level of p= 0.05 as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

According to further features in preferred embodiments of the invention described below the level of expression of the at least one gene or genes is determined by quantifying a level of a protein product thereof in the sample.

According to still further features in the described preferred embodiments quantifying a level of the protein is effected using a reagent which specifically binds with the protein.

According to yet further features in preferred embodiments of the invention described below the reagent comprises an antibody or fragments thereof.

According to further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table I.

According to still further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table II.

According to yet further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table III.

According to further features in preferred embodiments of the invention described below the at least one gene or genes are selected from the genes listed in Table IV.

According to still further features in the described preferred embodiments at least one gene or genes are selected from the genes listed in Table V.

According to yet further features in preferred embodiments of the invention described below the level of expression of the at least one gene or genes in the sample is determined by detecting the presence in the sample of a transcribed polynucleotide or portion thereof. The transcribed polynucleotide can be mRNA.

According to further features in preferred embodiments of the invention described below the transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with the transcribed polynucleotide or portion thereof.

According to still further features in the described preferred embodiments the sample from a subject is T cells, the at least one gene or genes are selected from the genes listed in Table IV and the normal expression of the gene or genes is T-cell expression.

According to still further features in the described preferred embodiments the at least one gene comprises at least 10, at least 50, at least 100, at least 250, at least 500, at least 750, at least 1000 or at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V.

According to another aspect of the present invention there is provided a kit for diagnosing multiple sclerosis in a subject, the kit comprising components suitable for determining expression levels of at least one gene selected from the group of genes listed in Tables I-V.

According to further features in the described preferred embodiments the reagents include at least one polynucleotide sequence selected capable of specifically hybridizing with an transcription product of the at least one gene and reagents for detecting and optionally quantifying a complex formed from the at least one polynucleotide sequence and said transcription product.

According to still further features in the described preferred embodiments the reagents include at least one antibody selected capable of specifically binding a polypeptide product of the at least one gene and reagents for detecting and optionally quantifying a complex formed from the at least one antibody and the polypeptide product.

According to further features in preferred embodiments of the invention described below the at least one gene is selected from the genes listed in Table I.

According to still further features in preferred embodiments of the invention described below the at least one gene is selected from the genes listed in Table II.

According to yet further features in preferred embodiments of the invention described below the at least one gene is selected from the genes listed in Table III.

According to further features in preferred embodiments of the invention described below the at least one gene is selected from the genes listed in Table IV.

According to still further features in the described preferred embodiments at least one gene is selected from the genes listed in Table V.

According to further features in preferred embodiments of the invention described below the kit further comprises packaging material identifying the kit as useful from diagnosing MS.

According to another aspect of the present invention there is provided a polynucleotide array comprising at least 10 and no more than 1500 polynucleotide sequences, wherein each of the sequences is selected capable of hybridizing with a transcription product of a polynucleotide sequence of a gene selected from the group of genes listed in Tables I-V.

According to further features in preferred embodiments of the invention described below the array is selected having polynucleotide sequences capable of diagnosing subjects suspected of suffering from multiple sclerosis. The

subjects may also be suspected of suffering from probable multiple sclerosis, primary progressive multiple sclerosis, secondary progressive multiple sclerosis, and/or relapsing/remitting multiple sclerosis.

According to further features in preferred embodiments of the invention described below the gene is selected from the genes listed in Table I, II, III, IV and/or IV.

According to yet another aspect of the present invention there is provided an array comprising at least 10 and no more than 1500 antibodies or antibody fragments each capable of specifically binding a protein product of a gene selected from the group of genes listed in Tables I-V.

According to further features in preferred embodiments of the invention described below the array is selected having antibodies or antibody fragments capable of diagnosing subjects suspected of suffering from multiple sclerosis. The subjects may also be suspected of suffering from probable multiple sclerosis, primary progressive multiple sclerosis, secondary progressive multiple sclerosis, and/or relapsing/remitting multiple sclerosis.

According to further features in preferred embodiments of the invention described below the gene is selected from the genes listed in Table I, II, III, IV and/or IV.

Implementation of the method and system of the present invention involves performing or completing selected tasks or steps manually, automatically, or a combination thereof. Moreover, according to actual instrumentation and equipment of preferred embodiments of the method and system of the present invention, several selected steps could be implemented by hardware or by software on any operating system of any firmware or a combination thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the

drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

FIGs. 1A-B are graphic representations of the differences in PMBC gene expression between MS patients and healthy subjects. RNA from Peripheral Blood Mononuclear Cells (PMBC) of 26 patients diagnosed with MS, and 18 healthy, age-matched controls was purified, labeled hybridized to a Genechip array (U95Av2, Affymetrix Inc. Santa Clara CA, USA), scanned and analyzed according to manufacturer's recommendations. The data were normalized and fold ratios calculated for each gene of the MS samples against the geometric mean of the controls. Figure 1A shows the number of MS specific genes detected having increased expression (fold change greater than 1.5) analyzed by t-test (red line), TNoM (green line) and INFO (blue line), compared with random occurrence (black line), at confidence levels (False Discovery Rates, FDR) of 90% ($p= 0.10$) to 100% ($p= 0$). Note the high level of significant MS-related gene expression at 95% FDR and above (arrows) (1249 distinguished genes). Figure 1B is an infogram of the 1249 genes most significantly ($p<0.05$ on all three tests) distinguishing MS patients (MS) from (control) healthy controls, determined as above. Each spot represents expression of a specific gene; color intensity of overexpressed (green) and under-expressed (red) genes indicates fold increase as compared to controls. Gray color indicates genes showing no difference in expression between MS and controls.

FIGs. 2A-B are graphic representations of the differences in PMBC gene expression between MS patients during acute relapse, and MS patients in remission. RNA from PMBC of 12 relapsed, and 14 clinically in remission patients was purified, labeled, hybridized and analyzed as described for Figures 1A-B hereinabove. Figure 2A shows the number of acute relapse-specific genes detected having increased expression in relapse, as analyzed by t-test (red line), TNoM (green line) and INFO (blue line), compared with random occurrence (black line), at confidence levels (False Discovery Rates, FDR) of 90% ($p= 0.10$) to 100% ($p= 0$). 735 genes were detected having significant relapsing-related gene expression at 95% FDR and above. Figure 2B is an infogram analysis of the 735 genes most significantly ($p<0.05$ on all three tests) distinguishing acute relapsing MS patients (Relapse) from MS patients in remission (Remission). Note the different profiles of gene expression in patients undergoing treatment (Relapse + and Remission +) compared with untreated patients (Relapse- and Remission -).

FIG. 3 is a pie chart diagram showing the breakdown, by functional character, of specific genes displaying up- or down-regulation in MS-derived MOG-reactive T-cell lines, as compared to normal-derived MOG-reactive T-cell lines. Significant MOG reactive MS-related genes are defined as genes with TNoM=0 and $p=0.057$ as compared to normal MOG-reactive T-cells.

FIG. 4 is a graphic representation of the differences in gene expression between MOG-stimulated T-cell lines from MS patients and healthy controls. RNA from MOG-stimulated T-cells of 4 MS patients and 3 matched controls was purified, labeled, hybridized and analyzed as described for Figures 1A-B hereinabove. Panel A shows a cluster analysis of 150 differentially expressed genes analyzed as described hereinabove (TNoM=0, $p<0.05$) distinguishing T-cells of MS (MS) patients from controls (Controls). Panel B shows a cluster analysis of the 43 most informative genes (TNoM=0, $p<0.05$, and fold change> 1.5). Each row represents a gene, and each column represents a T-cell line form a different subject. Yellow color indicates genes with an increased

expression relative to controls are yellow, and blue color indicates genes with relative decreased expression.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of methods and kits for diagnosing multiple sclerosis in subjects, using novel gene expression profiles derived from peripheral blood cells. Specifically, the present invention can be used to diagnose MS in early stages of the disease, to determine clinical stage and predict the course of the disease in patients with a unclear diagnoses, to provide definition and prognostic information in patients with probable MS, to assess and monitor MS therapies and to screen new and established drugs and treatments for MS.

The principles and operation of the present invention may be better understood with reference to the drawings and accompanying descriptions.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the Examples and drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

The present invention provides previously unavailable accuracy in predicting and staging MS, by identifying genes and groups of genes specifically over- and under-expressed in PBMC of patients at various stages of their disease.

As is further described in the Examples section which follows, the present inventors have conducted a broad scale analysis of PMBC expressed genes using hybridization of biotin-labeled PBMC mRNA to more than 12,000 human gene sequences provided on DNA chips. By utilizing specialized

statistical analysis approaches, the present inventors identified in the microarray data the most highly informative expression profiles.

As mentioned hereinabove, multiple sclerosis is a chronic, multi-factorial neurodegenerative disease of unknown etiology, the diagnosis and classification of which remains largely clinical in nature. Identification of the stages and progression of the disease, particularly definition of the probable MS stage, is crucial to determination of optimal treatment regimen and development of effective therapies. However, the complexities of autoimmune interactions, and the variability of MS in different individuals have made diagnosis and subsequent prognosis using traditional methods inexact and challenging. Methods for more accurate diagnosis of MS are greatly needed.

The profiles of MS-related genetic markers listed in Table I represent genes exhibiting differential expression in PBMCs from a large sample of MS patients, compared to that of age-matched healthy controls. Abundance of specific gene transcripts, represented by the intensity of label hybridizing to individual sequence loci of the MicroArray (Affymetrix Inc, Santa Clara CA), was recorded and quantified according to the manufacturers recommended protocols (such as GeneChip 3.0 software from Affymetrix). However, rather than composing the profile of differentially expressed genes based on probabilities using simple distribution of mean intensities, as has been reported by Ramanathan et al (J Immunol 2001;116:213-219), informative genes were selected based on the degree to which they were predictive of classification of the sample as "diseased" or "not diseased". By applying the rigorous three-pronged statistical analysis described in detail hereinbelow, 1249 genes most informative in distinguishing between diseased and otherwise not diseased patients were identified (see Table I). By applying an even more restrictive analysis of the data in Table I (see Table II, Bonfferoni analysis), a subset of the 300 highest scoring genes was identified. These MS marker genes comprise both over-expressed and downregulated genes, and represent of a diverse group of functional gene categories. Additional analysis of the markers

uncovered herein also led to the identification of another restricted marker set which can be accurately utilized to diagnose probable MS patients. As is further described hereinbelow, the identification of such a marker set represents a significant breakthrough since it enables to treat individuals at a much earlier stage of MS then previously possible.

Thus, according to one aspect of the present invention there is provided a method of diagnosing a subject with multiple sclerosis by determining a level of expression of at least one gene of the genes listed in Tables I-V in a sample obtained from the subject, wherein a substantial difference between the level of expression of the gene in the sample obtained from the subject and a normal expression level of the gene is an indication that the subject is afflicted with multiple sclerosis.

Normal expression levels of a marker or markers are obtained from isolated or cultured PMBCs (e.g., T-cell cultures), or samples obtained from individuals not affected with MS. A substantial difference is preferably of a magnitude that is statistically significant (see the Examples section for more detail). In particularly preferred embodiments, the marker is increased or decreased relative to control samples by at least 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, or 10-fold or more. Similarly, one skilled in the art will be well aware of the fact that a preferred detection methodology is one in which the resulting detection values are above the minimum detection limit of the methodology utilized.

As is further described in the Examples section which follows, the marker listed in Tables I-V were identified in peripheral blood cells. As such, the sample obtained from the individual is preferably a peripheral blood sample or any sample which includes blood cells such as T-cells. In a preferred embodiment, the sample is blood, thymus, spleen, lymph, pus, or bone marrow. However, it will be apparent to one skilled in the art that PMBCs may be present as an infiltrate in many other tissues, and that such tissues may also serve as samples in which the presence, activity, and/or quantity of the markers of the invention may be assessed. The tissue samples containing one or more of

the markers themselves may be useful in the methods of the invention, and one skilled in the art will be well aware of methods by which such samples may be conveniently obtained, stored, preserved and processed. For further description relating to collection and processing of blood samples please see the Examples section which follows.

As is detailed in the Examples section below, analysis of PBMC genes differentially expressed in MS, according to the methods described herein, revealed groups of genes of specific interest in MS. Genes that are most significantly over expressed, or downregulated in MS can indicate members of pathways important to disease development or pathology. Strongly overexpressed genes, according to Tables I and II, include **SLAM** (signaling lymphocyte activation molecule, GenBank Accession No. U33017), **LEF1** (lymphoid enhancer-binding factor 1, GenBank Accession No. AL099409), **LRP5** (low density lipoprotein receptor-related protein 5, GenBank Accession No. AF077820), **LILRB** (leukocyte immunoglobulin-like receptor, GenBank Accession No. AF004230), **LY75** (lymphocyte antigen 75, GenBank Accession No. AF011333), **CDW52** (GenBank Accession No. N90866), **PIP5K1-gamma** (Phosphatidylinositol-4-phosphate 5-kinase, type 1, gamma, GenBank Accession No. AB011161), **MAP4** (Microtubule-associated protein 4, GenBank Accession No. M64571), **CTSK** (Cathepsin K, GenBank Accession No. X82153) and **CTSB** (Cathepsin B, GenBank Accession No. L22507). Strongly down-regulated genes include **IL1B** (Interleukin 1 beta, GenBank Accession No. M15330), **TRAF6** (GenBank Accession No. U78798), **SCYA20** (GenBank Accession No. U64197), **IL1R** (type1 receptor, GenBank Accession No. M27492), **IL1RAP** (receptor accessory protein, GenBank Accession No. AB006537) and **IL1RN** (receptor antagonist, GenBank Accession No. X52015), **TGFB1** (Transforming growth Factor beta 1, GenBank Accession No. X05839), **SKI** (v-ski sarcoma viral oncogene homologue, GenBank Accession No. X15218), **VEGF** (Vascular endothelial

growth factor, GenBank Accession No. M63978), **IGFBP4** (Insulin-like growth factor binding protein 4, GenBank Accession No. U20982), **EREG** (epiregulin, GenBank Accession No. NM_001432.1), and **NR4A1, NR4A2, NR4A3** (nuclear receptor family genes, GenBank Accession Nos. NM_002135.1, X75918 and U12767, respectively).

Functional groups of genes strongly represented in the profile of most significantly differentially regulated genes in MS include, inter alia, apoptosis-related genes, T-cell activation and expansion related genes, cell proliferation related genes and epidermal growth factor genes. Many of the marker genes identified are associated with other MS- related genes, according to Tables I-V.

It will be appreciated that although a single marker can be used for diagnosis, diagnostic accuracy typically increases with an increase in the number of markers utilized.

As such, the diagnostic method of the present invention preferably utilizes a marker set that can range anywhere from 2 genes to 1200 genes. For example, the present method can utilize at least 10, at least 50, at least 100, at least 250, at least 500, at least 750, at least 1000 or at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V. Most preferably the markers utilized are selected from the sequences listed in Table II.

The markers sets utilized can be selected according to a statistical significance or fold change thereof (provided for each marker in Tables I-V), a higher significance and higher fold change indicating higher probability of marker accuracy. For example, a selected marker set can encompass markers displaying a high statistical significance (low P-value), preferably a P-value lower than 5.0E-02, more preferably lower than 5.0E-04, most preferably, lower than 5.0E-06. Alternatively, markers can be selected according to shared features of the marker gene. For example, gene markers of similar cellular function (e.g., genes of a signaling pathway such as apoptosis) or markers

displaying similar activity (e.g., enzymes of the same enzyme family) can be grouped into specific marker sets.

Each marker set may be considered individually, although it is within the scope of the invention to provide combinations of two or more marker sets for use in the methods and compositions of the invention to increase the confidence of the analysis.

As used herein, the terms "polynucleotide" and "oligonucleotide" are used interchangeably, and include polymeric forms of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. Polynucleotides may have any three-dimensional structure, and may perform any function, known or unknown. The following are non-limiting examples of polynucleotides: a gene or gene fragment, exons, introns, messenger RNA (mRNA), transfer RNA, ribosomal RNA, ribozymes, cDNA, recombinant polynucleotides, branched polynucleotides, plasmids, vectors, isolated DNA of any sequence, isolated RNA of any sequence, nucleic acid probes, and primers. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. If present, modifications to the nucleotide structure may be imparted before or after assembly of the polymer. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The term also includes both double- and single-stranded molecules. Unless otherwise specified or required, any embodiment of this invention that is a polynucleotide encompasses both the double-stranded form and each of two complementary single-stranded forms known or predicted to make up the double-stranded form.

As used herein, a "gene" includes a polynucleotide containing at least one open reading frame that is capable of encoding a particular polypeptide or protein after being transcribed and translated. Any of the polynucleotide sequences described herein may be used to identify larger fragments or full-length coding sequences of the gene with which they are associated. Methods

of isolating larger fragment sequences are known to those of skill in the art, some of which are described herein. A "gene product" includes an amino acid (e.g., peptide or polypeptide) generated when a gene is transcribed and translated.

As used herein, a "probe" is defined as an oligonucleotide that is provided as a reagent to detect a target present in a sample of interest by hybridizing with the target. Usually, a probe will comprise a label or a means by which a label can be attached, either before or subsequent to the hybridization reaction. Suitable labels include, but are not limited to radioisotopes, fluorochromes, chemiluminescent compounds, dyes, and proteins, including enzymes.

As used herein, "expression" includes the process by which polynucleotides are transcribed into mRNA and translated into peptides, polypeptides, or proteins. "Differentially expressed", as applied to a gene, includes the differential production of mRNA transcribed from a gene or a protein product encoded by the gene. A differentially expressed gene may be overexpressed or underexpressed as compared to the expression level of a normal or control cell. In one aspect, it includes a differential that is 2.5 times, preferably 5 times or preferably 10 times higher or lower than the expression level detected in a control sample. The term "differentially expressed" also includes nucleotide sequences in a cell or tissue which are expressed where silent in a control cell or not expressed where expressed in a control cell.

As used herein, the term "polypeptide" is defined as a compound of two or more subunit amino acids, amino acid analogs, or peptidomimetics. The subunits may be linked by peptide bonds. In another embodiment, the subunit may be linked by other bonds, e.g., ester, ether, etc. As used herein the term "amino acid" includes either natural and/or unnatural or synthetic amino acids, including glycine and both the D or L optical isomers, and amino acid analogs and peptidomimetics. A peptide of three or more amino acids is commonly

referred to as an oligopeptide. Peptide chains of greater than three or more amino acids are referred to as a polypeptide or a protein.

As used herein, the term "marker" is defined as a polynucleotide or polypeptide molecule which is present or absent, or increased or decreased in quantity or activity in subjects afflicted with multiple sclerosis, or in cells involved in multiple sclerosis. The relative change in quantity or activity of the marker is correlated with the incidence or risk of incidence of multiple sclerosis or progression from one stage of the disease to another.

Although all of the markers listed in Tables I-V can be used in diagnosis of MS, an additional object of the present invention was to identify those markers which can be utilized to diagnose specific clinical forms and/or stages of MS.

Accurate clinical tools for specific diagnosis of disease stages in MS are presently unavailable.

As a result of comprehensive studies conducted in efforts to evaluate specific gene expression in relation to clinical disease phases, the present invention provides, for the first time, specific markers sets which can be utilized in accurate diagnosis of specific forms and stages of MS

As is illustrated in Example II of the Examples section which follows, the present invention provides marker sets which can be accurately utilized to diagnose acute relapse, remission and probable stages of MS (Tables III-V).

Of particular importance is the marker set provided in Table V. As is described in the Examples section which follows, the present inventors also uncovered cellular markers which distinct between disease-related and non-disease related T-cell myelin reactivity. Although MS appears to be caused by autoimmune T-cells activated against myelin self-antigens, myelin-reactive T-cells have been demonstrated in healthy subjects as well. Thus, distinction between disease-related and non-disease related T-cell myelin reactivity is of great clinical and investigational importance.

Cellular markers which distinct between disease-related and non-disease related T-cell myelin reactivity include down-regulating apoptosis associated genes, up regulating anti-apoptotic genes and genes responsible for increased expansion capability of autoreactive T cells and enhanced ability to penetrate the CNS. Thus, the markers of Table V include genes involved in perpetuating pathologic cellular proliferation and tissue destruction within the CNS characteristic of MS, along with increased resistance to regulation. This marker set accurately defines the requirements for an individual to develop MS, and thus has important predictive value, especially in diagnosing individuals having MS in the "probable" stage.

The identification of these markers significantly advances the field of MS diagnosis and treatment as well as provides tools which will enable elucidation of the mechanisms underlying MS formation and progression, ultimately leading to formulation of efficient, stage specific, treatment regimens.

The markers of the invention may be nucleic acid molecules (e.g., DNA, cDNA, or RNA) or the polypeptides encoded thereby. As such, detection of markers in a sample obtained from an individual can be effected using various detection methods well known to the ordinary skilled artisan.

Briefly, measurement of the relative amount of nucleic acid or polypeptide molecules can be effected by any method known in the art (see, e.g., Sambrook, J., Fritsh, E. F., and Maniatis, T. Molecular Cloning: A Laboratory Manual. 2nd, ed, Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989; and Current Protocols in Molecular Biology, eds. Ausubel et al. John Wiley & Sons: 1992). Typical methodologies for RNA detection include RNA extraction from a cell or tissue sample, followed by hybridization of a labeled probe (e.g., a complementary nucleic acid molecule) specific for the target RNA to the extracted RNA, and detection of the probe (e.g., Northern blotting). Typical methodologies for polypeptide detection include activity assays in cases of

known enzymes, protein extraction from a cell or tissue sample, followed by hybridization of a labeled probe (e.g., an antibody) specific for the target protein to the protein sample, and detection of the probe. The label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Detection of specific polypeptide and nucleic acid molecules may also be assessed by gel electrophoresis, column chromatography, direct sequencing, or quantitative PCR (in the case of nucleic acid molecules) among many other techniques well known to those skilled in the art.

Probes based on the nucleotide sequence of a marker gene or of a nucleic acid molecule encoding a marker polypeptide of the invention can be used to detect transcripts or genomic sequences corresponding to the marker gene(s) and/or marker polypeptide(s) of the invention. In preferred embodiments, the probe comprises a label group attached thereto, e.g., the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissue which misexpress (e.g., over- or under-express) a marker polypeptide of the invention, or which have greater or fewer copies of a marker gene of the invention. For example, a level of a marker polypeptide-encoding nucleic acid in a sample of cells from a subject may be detected, the amount of mRNA transcript of a gene encoding a marker polypeptide may be determined, or the presence of mutations or deletions of a marker gene of the invention may be assessed. The invention further encompasses nucleic acid molecules that differ from the nucleic acid sequences of the genes set forth in Tables I-V, due to degeneracy of the genetic code and which thus encode the same proteins as those encoded by the genes shown in Tables I-V.

An isolated marker protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind marker proteins using standard techniques for polyclonal and monoclonal antibody preparation. A full-length marker protein can be used or, alternatively, the invention provides antigenic peptide fragments of these proteins for use as immunogens. The

antigenic peptide of a marker protein comprises at least 8 amino acid residues of an amino acid sequence encoded by a gene set forth in Tables I-V, and encompasses an epitope of a marker protein such that an antibody raised against the peptide forms a specific immune complex with the marker protein. Preferably, the antigenic peptide comprises at least 10 amino acid residues, more preferably at least 15 amino acid residues, even more preferably at least 20 amino acid residues, and most preferably at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the marker protein that are located on the surface of the protein, e.g., hydrophilic regions, as well as regions with high antigenicity.

An anti-marker protein antibody (e.g., monoclonal antibody) can be used to isolate a marker protein of the invention by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-marker protein antibody can facilitate the purification of natural marker proteins from cells and of recombinantly produced marker proteins expressed in host cells. Moreover, an anti-marker protein antibody can be used to detect marker protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the marker protein. Anti-marker protein antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material

includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S or ^{3}H.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (J. Mol. Biol. 1990;215:403-10). BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to marker protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See http://www.ncbi.nlm.nih.gov.

It will be appreciated that non-coding sequences, such as promoter or other regulatory sequences of marker genes may be used as probes in the context of the present invention. Thus, the expression of groups of functionally related genes, responsive to similar signals important to the pathogenesis or progression of multiple sclerosis, may be assessed.

It will be appreciated that in certain cases the genes themselves can serve as markers. For example, mutations in the nucleic acid sequence of a gene (e.g., non-sense, mis-sense deletion and the like) which result in lower expression levels of the gene or lower activity of the gene product may be correlated with MS. Similarly, a duplication of the gene, which can result in higher expression levels or mutations which result in higher activity can also be correlated with MS.

Detection of the presence or number of copies of all or a part of a marker gene of the invention may be performed using any method known in the art. Typically, it is convenient to assess the presence, quantity and quality of genomic DNA by Southern analysis, in which total DNA from a cell or tissue sample is extracted, is hybridized with a labeled probe (e.g., a complementary DNA molecule), and the probe is detected. The label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Other useful methods of DNA detection and/or quantification include direct sequencing, gel electrophoresis, column chromatography, and quantitative PCR, as is known by one skilled in the art.

In cases where detection involves discrete marker sets, the detection method of the present invention preferably employs marker probes which are conjugated to a solid support. For example, polynucleotide probes capable of specifically hybridizing with polynucleotide markers of the present invention (e.g., mRNA) may be coupled to an array (e.g., a GeneChip array for hybridization analysis), to a resin (e.g., a resin which can be packed into a column for column chromatography), or a matrix (e.g., a nitrocellulose matrix for northern blot analysis). The immobilization of molecules complementary to the marker(s), either covalently or noncovalently, permits a discrete analysis of the presence or activity of each marker in a sample. In an array, for example, polynucleotides complementary to each member of a marker set may individually be attached to different, known locations on the array (region-specific arrays). The array may be hybridized with, for example, polynucleotides extracted from a blood sample obtained from a subject. The hybridization of polynucleotides extracted from the sample with the array at any location on the array can be detected, and thus the presence or quantity of the marker in the sample can be ascertained. In a preferred embodiment, a "GeneChip" array is employed (e.g., an Affymetrix type array). Similarly, Western analyses may be performed on immobilized antibodies specific for different polypeptide markers hybridized to a protein sample from a subject.

It will also be apparent to one skilled in the art that the probes of the array need not bind with the entire marker molecule. A probe designed to bind a portion of the marker of sufficient length for detection purposes (e.g., for hybridization), for example, a portion of the marker which is 7, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 100 or more nucleotides or amino acids in length may be sufficient for detection purposes.

Polynucleotide probes can be synthesized using any known synthesis method. Preferably, synthesis is effected using on-chip lithography methodology in a manner similar to that utilized for the synthesis of Affymetrix chips (www.affymetrix.com). Additional methods of array production and methodology are described in detail in the U.S. Patent Applications cited in the Background section hereinabove.

Antibody probes useful for detecting polypeptide markers can be generated using various well known techniques. For example, monoclonal antibodies which can be used per se or as a basis for antibody fragments (scFv, Fab etc) can be synthesized using isolated Hybridomas. In such an approach, a protein corresponding to a marker of the invention is isolated (e.g., by purification from a cell in which it is expressed or by transcription and translation of a nucleic acid encoding the protein in vivo or in vitro using known methods. A vertebrate, preferably a mammal such as a mouse, rat, rabbit, or sheep, is immunized using the isolated protein or protein fragment. The vertebrate may optionally (and preferably) be immunized at least one additional time with the isolated protein or protein fragment, so that the vertebrate exhibits a robust immune response to the protein or protein fragment. Splenocytes are isolated from the immunized vertebrate and fused with an immortalized cell line to form hybridomas, using any of a variety of methods well known in the art. Hybridomas formed in this manner are then screened using standard methods to identify one or more hybridomas which produce an antibody which specifically binds with the protein or protein fragment.

The invention also includes an array comprising a marker(s) of the present invention. The array can be used to assay expression of one or more genes in the array.

In one embodiment, the array can be used to assay gene expression in a tissue of multiple sclerosis patients at different stages of the disease to ascertain stage specificity of genes in the array. In this manner, more than about 30,000 genes can be simultaneously assayed for expression. This allows a profile to be developed showing a battery of genes specifically expressed in one or more stages of the disease.

In addition to such qualitative determination, the invention allows the quantitation of gene expression. Thus, not only stage specificity, but also the level of expression of a battery of stage specific genes is ascertainable. Thus, genes can be grouped on the basis of their expression per se, and level of expression in that stage of the disease.

The detection arrays described herein are preferably packaged in kits identified for use in detecting MS in general or for detecting specific stages of MS. The kit can further include reagents suitable for the detection of polynucleotide hybridization or antibody binding and instructions for effecting diagnosis using the kit components and suitable detection hardware (e.g., detection microscope) and software (e.g., detection and analysis software). For further description of such hardware and software and detection reagents please see www.affymetrix.com.

Thus, the present invention provides methods useful for diagnosing MS including specific stages or states of the disease and also a risk of developing the disease.

These methods involve isolating a sample from a subject (e.g., a sample containing T-cells), detecting the presence, quantity, and/or activity of one or more markers of the invention in the sample relative to a normal sample. Observing a significant increase or decrease in one or more markers in the test sample indicates the presence or risk of presence of MS.

Using specific marker sets, the present invention also provides methods of assessing the severity or stage of MS in a subject.

As detailed hereinabove, a major concern in treatment of multiple sclerosis is accurate early diagnosis following the first acute attack. At present, clinical studies indicate that only 40-50% of individuals suffering a first acute attack will progress to clinically definite MS. Thus, treatment protocols most commonly suspend treatment of these patients defined as probable MS, until the appearance of a second attack, which may entail years of waiting and uncertainty. It will be appreciated that early and accurate detection of the portion of probable MS patients likely to progress to further stages of the disease can save undue suffering and expense, and, more importantly, provide early treatment and a better prognosis for the portion of probable MS patients likely to progress to more severe stages. The present invention provides, for the first time, marker genes for probable MS, as well as for relapsing vs. remitting MS.

The present invention also provides methodology which can be used to assess the efficacy of an MS treatment regimen and/or the effect of environmental factors or diet on the progression of MS.

These methods involve isolating a sample from a subject (e.g., a sample containing T-cells) suffering from MS who is undergoing treatment which includes drug therapy, exposure to a predetermined environmental condition and/or a specific diet, detecting the presence, quantity, and/or activity of one or more markers of the invention in test samples obtained from the subject prior to and following treatment or in a test sample obtained from the subject relative to a sample obtained from an individual suffering from MS who is not undergoing any treatment and/or relative to a sample obtained from an individual not suffering from MS and undergoing treatment. The levels of markers in the samples are compared, and significant increases or decreases in one or more markers in the test sample following treatment relative to the other samples are observed, and correlated with the severity or stage of MS. By assessing whether

MS has been lessened or alleviated, the ability of the treatment or therapy to treat MS is also determined.

It will be appreciated that the present invention also provides methods of treating (e.g., inhibiting) the formation or progression of MS. These methods involve isolating a sample from a subject (e.g., a sample containing PMBCs such as T-cells), detecting the presence, quantity, and/or activity of one or more markers of the invention in the sample relative to a normal sample and observing significant increases or decreases in one or more markers in the test sample. For markers that are significantly decreased in expression or activity, the subject may be administered that expressed marker protein, or may be treated by the introduction of mRNA or DNA corresponding to the decreased marker (e.g., by gene therapy), to thereby increase the levels of the marker protein in the subject. For markers that are significantly increased in expression or activity, the subject may be administered mRNA or DNA antisense to the increased marker (e.g., by gene therapy), or may be administered antibodies specific for the marker protein, to thereby decrease the levels of the marker protein in the subject. In this manner, the subject may be treated for MS or MS related condition.

In another embodiment, the methods further involve obtaining a control biological sample (e.g., nondiseased tissue) from a control subject, contacting the control sample with a compound or agent capable of detecting marker protein, mRNA, or genomic DNA, such that the presence of marker protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of marker protein, mRNA or genomic DNA in the control sample with the presence of marker protein, mRNA or genomic DNA in the test sample.

The invention also provides methods for identifying modulators, i.e., candidate or test compounds or agents (e.g., peptides, peptidomimetics, peptoids, small molecules or other drugs) which (a) bind to the marker, or (b) have a modulatory (e.g., stimulatory or inhibitory) effect on the activity of the

marker or, more specifically, (c) have a modulatory effect on the interactions of the marker with one or more of its natural substrates (e.g., peptide, protein, hormone, co-factor, or nucleic acid), or (d) have a modulatory effect on the expression of the marker. Such assays typically comprise a reaction between the marker and one or more assay components. The other components may be either the test compound itself, or a combination of test compound and a natural binding partner of the marker. The test compounds of the present invention may be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. Test compounds may also be obtained by any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive; (see, e.g., Zuckermann et al., 1994, J. Med. Chem. 37:2678-85); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the `one-bead one-compound` library method; and synthetic library methods using affinity chromatography selection. The biological library and peptoid library approaches are limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, 1997, Anticancer Drug Des. 12:145).

Additional objects, advantages, and novel features of the present invention will become apparent to one ordinarily skilled in the art upon examination of the following examples, which are not intended to be limiting. Additionally, each of the various embodiments and aspects of the present invention as delineated hereinabove and as claimed in the claims section below finds experimental support in the following examples.

EXAMPLES

Reference is now made to the following examples, which together with the above descriptions, illustrate the invention in a non limiting fashion.

Generally, the nomenclature used herein and the laboratory procedures utilized in the present invention include molecular, biochemical, microbiological and recombinant DNA techniques. Such techniques are thoroughly explained in the literature. See, for example, "Molecular Cloning: A laboratory Manual" Sambrook et al., (1989); "Current Protocols in Molecular Biology" Volumes I-III Ausubel, R. M., ed. (1994); Ausubel et al., "Current Protocols in Molecular Biology", John Wiley and Sons, Baltimore, Maryland (1989); Perbal, "A Practical Guide to Molecular Cloning", John Wiley & Sons, New York (1988); Watson et al., "Recombinant DNA", Scientific American Books, New York; Birren et al. (eds) "Genome Analysis: A Laboratory Manual Series", Vols. 1-4, Cold Spring Harbor Laboratory Press, New York (1998); methodologies as set forth in U.S. Pat. Nos. 4,666,828; 4,683,202; 4,801,531; 5,192,659 and 5,272,057; "Cell Biology: A Laboratory Handbook", Volumes I-III Cellis, J. E., ed. (1994); "Culture of Animal Cells - A Manual of Basic Technique" by Freshney, Wiley-Liss, N. Y. (1994), Third Edition; "Current Protocols in Immunology" Volumes I-III Coligan J. E., ed. (1994); Stites et al. (eds), "Basic and Clinical Immunology" (8th Edition), Appleton & Lange, Norwalk, CT (1994); Mishell and Shiigi (eds), "Selected Methods in Cellular Immunology", W. H. Freeman and Co., New York (1980); available immunoassays are extensively described in the patent and scientific literature, see, for example, U.S. Pat. Nos. 3,791,932; 3,839,153; 3,850,752; 3,850,578; 3,853,987; 3,867,517; 3,879,262; 3,901,654; 3,935,074; 3,984,533; 3,996,345; 4,034,074; 4,098,876; 4,879,219; 5,011,771 and 5,281,521; "Oligonucleotide Synthesis" Gait, M. J., ed. (1984); "Nucleic Acid Hybridization" Hames, B. D., and Higgins S. J., eds. (1985); "Transcription and Translation" Hames, B. D., and Higgins S. J., eds. (1984); "Animal Cell Culture" Freshney, R. I., ed. (1986); "Immobilized Cells and Enzymes" IRL Press, (1986); "A Practical

Guide to Molecular Cloning" Perbal, B., (1984) and "Methods in Enzymology" Vol. 1-317, Academic Press; "PCR Protocols: A Guide To Methods And Applications", Academic Press, San Diego, CA (1990); Marshak et al., "Strategies for Protein Purification and Characterization - A Laboratory Course Manual" CSHL Press (1996); all of which are incorporated by reference as if fully set forth herein. Other general references are provided throughout this document. The procedures therein are believed to be well known in the art and are provided for the convenience of the reader. All the information contained therein is incorporated herein by reference.

MATERIALS AND METHODS

Subjects - Blood was obtained from patients or controls after written informed consent. *For comparison of healthy controls and MS patients, and between MS patients in acute relapse or remission*: Gene expression profiles of 26 patients (20 females, mean age 41.0±2.5 years) with definite diagnosis of MS according to Poser criteria (8), a relapsing-remitting disease course, and brain magnetic resonance imaging ascertaining the diagnosis (9) were compared with eighteen (18) age-matched healthy subjects (16 females). *For comparison of transcriptional profiles in MOG-reactive T-cells*: Four MS female patients (mean age 38±4.2 years, mean disease duration 9.3±3.3 years) having a definite MS according to Poser criteria (10), a relapsing-remitting disease course, neurological disability evaluated by the expanded disability status scale (EDSS, 11) between 2 to 5.0, and brain MRI supporting the diagnosis of MS, and three age- and sex-matched healthy controls were included in the study. None of the patients received immunomodulatory drugs or steroid treatment for at least three months prior to when blood was drawn. The studies were approved by the institutional review board and the Israel Ministry of Health.

mRNA preparation - Total RNA was isolated from Ficoll™ isolated Peripheral Blood Mononuclear Cells (PBMC) or from MOG-stimulated T cell

lines ($2x10^7$ cells) by ice-cold TRIZOL Reagent (Gibco, BRL). Poly-A mRNA was isolated using a mini-kit (Oligotex, Qiagen) and used as a template for double-stranded cDNA synthesis using oligo (dT)-24 primers containing a T7 RNA polymerase promoter site added to the 3'- end (Genset). After phenol/chloroform extraction cDNA was used as a template for *in vitro* transcription (Ambion T7 Megascript system) with biotin labeled nucleotides (Enzo Diagnostics). Labeled cRNA was fragmented, quantified by spectrophotometer, and hybridized to the microarrays.

Microarray gene analysis - Each Genechip (U95Av2) which carries probes for 12,625 (or U133A with 22,000 for patients with probable MS diagnosis) transcripts was hybridized with 10μg/200μl hybridization mix, stained and scanned (Hewlett Packard, GeneArray-TM scanner G2500A) according to manufacturer protocol (Affymetrix Inc, Santa Clara, CA). Scaling procedure was performed to an average intensity of 600 per gene. A value of 20 was assigned to all measurements lower then 20. *For comparison of healthy controls and MS patients, and between MS patients in acute relapse or remission*: All data was normalized by dChip software and fold ratios were calculated for each gene of the samples against geometric means of the matched controls. *For comparison of transcriptional profiles in MOG-reactive T-cells*: Genes that did not have at least one average difference intensity value $\geq$100 or were present at least once by Affymetrix criteria, were not included in the analysis.

Data analysis - The analysis was performed according to the analytical approach as previously described (24-26). Genechip 4 software (Affymetrix Inc, Santa Clara, CA) was used for analysis of the scanned arrays. Fold ratios were calculated for each gene of the samples against the geometric mean of matched controls. *For comparison of transcriptional profiles in MOG-reactive T-cells*: To determine the most informative genes threshold number of misclassifications (TNoM) score was applied. This score counts the number of classification errors that occur between compared groups for each gene of the

dataset. The best threshold (TNoM=0) implies that no errors have been counted and the distinction between the two groups in relation to the expression level of a specific gene is maximal. To select a group of strongly differential expression, t-test p-value (comparing expression levels of genes from MS patients vs. healthy controls) were also computed. Genes with TNoM = 0, fold-change >1.5 (either up or down regulated) and corresponded t-test P value < 0.05, were designated as most informative. *For comparison of healthy controls and MS patients, and between MS patients in acute relapse or remission*: The data was analyzed by the classic parametric t-test, and the following non-parametric tests: (i) Threshold number of misclassifications (TNoM) method and (ii) INFO score that measures the misclassifications made by a simple threshold in terms of the information lost. Analysis was performed between MS patients and the control group for each gene of the dataset as well as between subgroups of patients. Only informative MS related genes ($p<0.05$ in all three statistical tests) were included. To retrieve the most informative genes, the False Discovery Rate (FDR) method (14) that ranks and tests all "P" values against different thresholds was used. The degree of significance by the Bonferroni threshold method, which evaluates the allowed error probability divided by the number of genes measured, and ensures that each and every validated scoring event is indeed a significant event, was also calculated.

Validation Strategy - To further assess the predictive power of the data sets, computerized analysis by the Leave-One-Out-Cross-Validation (LOOCV) statistical method was performed. The method simulates removal of a single sample every trial and trains on the rest. The procedure is repeated until each sample is left out once and the number of correct and incorrect predictions is counted.

EXAMPLE I

Accurate Gene Expression Profiles of MS

In order to provide an accurate, reliable profile of gene markers for diagnosis and evaluation of MS, DNA chip analysis was used to compare multiple gene expression patterns of PBMCs from patients with different clinical forms of MS. After informed consent blood was obtained from 26 patients (20 females, mean age 41.0±2.5 years) with definite diagnosis of MS according to Poser criteria, a relapsing-remitting disease course, and brain magnetic resonance imaging ascertaining the diagnosis. Eighteen age-matched healthy subjects (16 females) served as controls. PBMC gene expression of 12,625 human genes was analyzed as described hereinabove, using Ficoll™ for preparation of PBMCs and total RNA purification and sample preparation according to the instructions of Affymetrix, Inc (Affymetrix, Santa Clara CA, USA). In order to determine the most informative genes, unique computerized scoring methods, as yet not applied to analysis of data regarding MS, were employed. In brief, a gene is designated as informative based on the degree to which its tissue expression level is predictive of an independent classification of the tissue sample as "diseased" or "not diseased", as previously described by Ben-Dor et al (J Comput Biol 2000;7:559-63) and applied to the analysis of breast cancer and melanoma using cDNA arrays (for review see Freidman N et al Ernst Schering Res Found Wkshp 2002;38:109-31). The scores used in this study were:

TNoM (Total Number of Misclassifications) - the number of classification errors committed when using the best simple threshold to distinguish between two classes (diseased or not diseased) based on the expression levels of a specific gene.

INFO - an estimate of the uncertainty remaining about accuracy of a sample classification (diseased or not diseased) after the incorporation of predictions based on expression of an individual gene is given (a lower "INFO" score indicates a higher predictive value for a given gene).

Gaussian (t-test) - The overlap between distributions of expression levels for genes in two classes. The score is based on normality assumptions.

One of the advantages of the analytic methods used here is their amenability to rigorous statistical benchmarking. Using this unique analysis, the number of informative genes per score expected in a random classification can be calculated, and then this estimated number of high scoring (or informative) genes can be compared to the actual number of informative genes (per score) measured in a dataset.

Comparison of the gene expression profiles shows that gene expression of PBMC in MS patients is significantly different from that in healthy subjects. Under the null-hypotheses that the separation of the samples is random despite genetic heterogeneity between tested groups, observed significant overabundance of informative genes was observed (Fig. 1A). The difference between expected and observed number of genes with significant p value in all 3 statistical tests (t-test, TNoM, INFO) performed, indicates that the diversity in gene expression observed in PBMC is biologically significant.

The predictive power of the data sets results was assessed by performing computerized error estimates based on *leave-one-out cross validation* (LOOCV) trials. The results disclosed only 3 classification errors. This low rate of error estimates suggest that the gene expression signature in MS is reliable for the diagnosis of the disease using peripheral blood and confirms that the patterns we observed accurately represent significant biologic phenomena associated with MS. The false discovery rate (FDR) method distinguished 1249 most informative genes that pass 95% FDR on all three statistical tests (t-test, TNoM, INFO) at $p < 0.05$ (Fig. 1B and Table I).

Confirmation of gene microarray expression findings was performed by RT-PCR for the following five randomly selected genes: EGFL5, P44, GS3686, MX1 and CCR2. Significant correlations (coefficients ranged from 0.76 to 0.98) were found between the relative number of expression genes analysis and the RT-PCR profile. The data from microarray hybridizations was further tested

against the strict Bonferroni threshold method from all three statistical tests, as described hereinabove, resulting in 300 top scoring genes that distinguish between MS and healthy subjects. (Table II).

The 1249 most informative genes (681 up-regulated, 569 down-regulated, Table I) consist of inflammatory, apoptosis and cell signaling pathways components, cytokines, antigen presentation molecules and chemokines as well as number of expressed sequence tags (ESTs).

Over-expressed genes in MS - The most abundant over-expressed transcripts unique to MS include: (i) **SLAM** (signaling lymphocyte activation molecule) a member of the immunoglobulin gene superfamily that is involved in T-cell stimulation. SLAM potentiates T-cell expansion and was described as CD28 independent co-stimulatory molecule, selectively increasing interferon gamma production and dysregulating type 1 and type 2 cytokine production in MS upon T-cell receptor activation. The surprising observation of SLAM upregulation suggests an enhanced proliferation of autoreactive T cells in MS patients; (ii) **LEF1** (lymphoid enhancer-binding factor 1) one of the transcriptional factors expressed in pre-B and T cells, and known to be associated with T cell receptor (TCR) stimulation and apoptosis survival of pro-B cells (19); (iii) **LRP5** (low density lipoprotein receptor-related protein 5) a of cell receptor protein required for LEF1 activation; (iv) **LILRB** (leukocyte immunoglobulin-like receptor), a protein that binds MHC class I molecules and delivers a negative signal inhibiting killing by natural killer and regulatory T cells; (v) **LY75** (lymphocyte antigen 75) an endocytotic receptor used by dendritic cells to direct captured antigens from the extracellular space to a specialized antigen-processing compartment; and (vi) **CDW52**, a 21-28 kDa glycopeptide antigen expressed on lymphocytes and macrophages known to be a target for complement-mediated insult, inducing pro-inflammatory cytokine (e.g. TNF alpha and interferon gamma) production. Other up-regulated genes are members of the anti-apoptotic pathways, and include **PIP5K1-gamma**

(Phosphatidylinositol-4-phosphate 5-kinase, type 1, gamma) and **MAP4** (Microtubule-associated protein 4). Over-expression of transcripts belonging to the papain cysteine proteinase family **CTSK** (Cathepsin K) and **CTSB** (Cathepsin B) was also observed.

Down-regulated genes in MS - Abundant down-regulated transcripts unique to MS that were identified include **IL1B** (Interleukin 1 beta), an important inflammatory cytokine; **TRAF6,** which is essential for IL1 signaling; and **SCYA20,** known to be mediated by IL1B. Decreased mRNA expression of **IL1B** was strengthened by the down regulation of **IL1R** (type1 receptor), **IL1RAP** (receptor accessory protein) and **IL1RN** (receptor antagonist).

Other important down-regulated genes include **TGFB1** (Transforming growth Factor beta 1) and **SKI** (v-ski sarcoma viral oncogene homologue) a component of TGFB signaling pathway, both known to inhibit cell proliferation. Thus, their under expression may contribute to autoreactive T cell expansion. Members of epidermal growth factor family such as **VEGF** (Vascular endothelial growth factor), **IGFBP4** (Insulin-like growth factor binding protein 4) and **EREG** (epiregulin) were also down regulated. Additionally, mRNA expression of members of the steroid-thyroid receptors family including nuclear receptor subfamily 4, group A members 1, 2 and 3 (**NR4A1, NR4A2, NR4A3**) were significantly reduced. Down regulation of these genes may inhibit apoptosis through Fas ligand and tumor necrosis factor alpha or through early response of T-cell receptor induced apoptosis of thymocytes, thus mimicking positive selection.

Taken together, the identification of profiles of up- (overexpressed) and down regulated genes specific to MS indicates the suitability of the methods of the present invention for identifying validated and significant molecular signatures of PBMC gene expression in MS. While reducing the present invention to practice, it was observed that the specific disease related genes include transcripts involved in T cell activation and expansion and anti-

apoptotic mediators, indicating failure of apoptosis-related elimination of autoreactive T cells.

EXAMPLE II

Stage Specific Gene Expression Profiles of MS

Accurate clinical tools for specific diagnosis of disease stages in MS are presently unavailable. In order to provide a useful profile of the clinically defined stages of MS, specific gene expression was evaluated in relation to clinical disease phases. Significant overabundance was found between the number of observed and expected genes expressed in MS patients during an acute relapse and in remission (Fig. 2A). Using the methods described hereinabove, the 743 most informative genes (302 up-regulated and 441 down-regulated) with p-value < 0.05 in all three scores (t-test, TNoM, INFO) that differentiated relapse from remission (Fig 2B, Table III) were identified.

Over-expressed genes in acute relapse of MS, compared to patients in remission - The most informative over-expressed genes included **CTSL** (Lysosomal cystein protease L, cathepsin L) known to play a role in MHC class II antigen presentation, responsible for quantitative and qualitative difference in peptide repertoires displayed by MHC class II molecules, and having a regulatory role in epitope generation for antigens subsets. Moreover, in vitro, proteolytic **CTSL** processed myelin basic protein into more then 60 different 20-40-mers species, and myelin-associated glycoprotein was described as a substrate for **CTSL** like proteases. These data, taken together with our observation that **CTSL** mRNA was over expressed in the active stage of MS, offer a biochemical basis for the immunodominant epitope spreading implicated in the pathogenesis of MS. Also up-regulated is **SCYA2** (Monocyte specific chemoattractant protein, MCP1), essential for monocyte and NK cells recruitment to site of inflammatory injury. Augmented **SCYA2** expression level in the CNS has been identified at the onset of EAE. Other abundant up-regulated transcripts identified by the method of the present invention include

CD79A, DDIT3 (DNA-damage inducible transcript 3); **E2-EPF** (Ubiquitin carrier protein) and **COX6.**

Downregulated genes in acute relapse of MS, compared to patients in remission - From the downregulated gene transcripts in acute relapse vs. remission it is important to note several programmed cell death-related genes like **CCNG1** (Cyclin G1) identified as p53 dependent apoptosis; **PDCD2** (Programmed cell death 2) expressed in immature thymocytes; and **CTLA1** (Cytotoxic T lymphocyte associated serine esterase 1), crucial for the rapid induction of apoptosis by cytotoxic cells. Also prominently downregulated during acute relapse was **JAK1** (Janus kinase 1), a protein tyrosine kinase reported to be obligatory for several cytokines receptors, important for regulation of acute cellular response.

The results of the functional annotation of the transcriptional motifs that distinguish between acute MS relapse and remission suggest that many of the genes are involved in cellular recruitment and epitope spreading, as well as important to immunologic mechanisms related to escape from regulatory surveillance and augmentation of cell survival potential. Thus, it can be suggested that during the acute inflammatory process of the disease there is a failure of the immune regulatory cells to inhibit autoreactivity and the self-expansion of the non-restrained autoreactive T cells further lead to a vicious cycle of on going inflammatory activity.

It is evident from the gene-clustering map (Fig 2B) that during an acute relapse no significant differences are found between relapse treated vs. relapse untreated patients. Such a result is of great clinical significance, since this may indicate that during an acute MS exacerbation the major gene expression transcripts are related to relapse associated genes and the effect of therapy is negligible. However, during remission treatment effect was more pronounced and this effect on gene suppression in treated patients was evident.

Of even greater significance is the demonstration, for the first time, of a specific gene expression profile of the "probable" stage of MS. As described

hereinabove, "probable" MS precedes definitive clinical diagnosis, and is characterized by diverse neurological symptoms including unilateral loss of vision, true vertigo, ataxia, paresthesia, incontinence, diplopia, dysarthria or paralysis. Probable MS patients may suffer undiagnosed for years. In order to provide a method for accurate diagnosis of probable MS, in advance of onset of clinical symptoms, gene expression in PBMC samples of 13 probable MS patients were compared with that of samples from 5 age-matched healthy controls. RNA preparation, hybridization to MicroArray and analysis of results was performed as described for Examples 1 and 2, and in the Material and Methods section hereinabove.

As is shown in Table V, a specific "probable" MS profile of gene expression distinguishes PBMCs of diseased and healthy individuals.

Thus, there is demonstrated, for the first time, gene expression profiles providing criteria for distinguishing between stages of MS in humans, for example, between relapsing and remitting MS, probable MS and healthy individuals. Further, the groups of up- and down-regulated genes identified herein may be used for investigation of mechanisms of disease and disease progression in MS.

EXAMPLE III

Gene Expression Profiles in Treatment of MS

The effect of immunomodulatory treatment on gene expression in MS patients was investigated by comparison analysis of gene transcripts between treated and untreated patients. Suprisingly, despite the variety of immunomodulatory treatments and differences between patients in relation to treatment duration, the microarray methods described herein, treatment-related gene transcripts that differentiated between treated and untreated patients were detected. Treatment-specific gene expression is mainly associated with phosphorylation and signal transduction. Thus, gene microarray technology can

be a powerful tool in evaluating and monitoring clinical correlations of effects of treatment, and determining prognosis.

Thus, data presented herein demonstrate for the first time distinct and significant fingerprint cluster in MS patients that differentiates them from healthy subjects. Moreover, the stringent and specific fingerprint is predictive for the diagnosis of MS and is suitable for guiding the selection of patients for early treatment. Additionally, separate gene expression patterns were identified between acute MS relapse and remission, and treatment effects could also be identified. The methods described herein may also be used to offer superior insight into the biological mechanisms involved in the disease as well as improving functional gene characterization and transcription sites detection, important for identification of new targets for treatment and drug identification, such as T cell activation and expansion and anti-apoptotic genes like **SLAM**, **PIP5K1-g** and the **NR4A1-3** steroid-thyroid receptors subfamily.

EXAMPLE IV

Gene Expression Profiles of MOG-Reactive T-cells from MS Patients

Although MS appears to be caused by autoimmune T cells activated against myelin self-antigens, myelin-reactive T-cells have been demonstrated in healthy subjects as well. Thus, distinction between disease-related and non-disease related T-cell myelin reactivity is of great clinical and investigational importance. In order to determine a profile of MS-related T-cell genes, gene expression in MOG-reactive T-cells from 4 MS patients having relapsing-remitting disease course, positive Poser criteria, and neurological disability, and 3 healthy age-matched controls was compared.

Using the microarray methods described herein, gene expression patterns obtained in MOG reactive T cell lines from MS patients detected 150 transcripts with TNoM=0, p=0.057 compared to healthy subjects (Figure 4). These high scoring gene transcripts were defined as significant MOG reactive MS-related genes. Hierarchical clustering of gene expression patterns from MS

patients and healthy controls is presented in Figure 2, panel A. From the 150 genes with absolutely different expression levels, 43 most informative genes were further identified and clustered. These include 18 up-regulated and 25 down-regulated genes (Figure 2, panel B).

Investigation of the known biological function of these genes (Table V) shows a great diversity of activity (A Pie-chart diagram showing the functional groups of genes included in this evaluation is presented in Figure 3). Included are genes coding for proteins involved in the regulation and execution of apoptosis, growth factors, mediators of signal transduction pathways, molecules that participate in inflammation and also genes encoding heat shock proteins, transcription factors and components of different biochemical pathways.

Upregulated Genes in MS-Derived T-cells - Up-regulated in MS patient-derived T-cell lines are several anti-apoptotic genes such as **BCL2, lifeguard**, and the MAP-activated kinase **MAP3K12**. The **BCL2** gene product is an important member of the anti-apoptotic proteins. Lifeguard (**LFG**), is a molecule that inhibits cell death mediated by the Fas (CD95) receptor through a unique mechanism that down regulates apoptotic signals from Fas and is associated with human autoimmune lymphoproliferative syndrome (ALPS) and in lymphoproliferative lupus-like syndrome in mice.

The MAP3K12 gene is associated with programmed cell death and encodes a polypeptide that catalyzes the phosphorylation of BAD, a member of the BCL2 anti-apoptosis protein family. Increased expression of **IGFBP3** and **VEGF** was also demonstrated in MS-derived T cells. **IGFBP-3** has been implicated in the expansion of disease related T-cell, associated with acute brain lesions of MS patients. Thus, in addition to increased survival potential, our findings suggest that autoreactive T cells in MS also have an expansion advantage compared with T cells from healthy individuals.

Furthermore, migration of autoimmune T cells into the brain would be expected to be assisted by over-expression of transcripts encoding for vascular

endothelial growth factor (**VEGF**) in lines from MS patients. **VEGF** enhances vascular permeability and may facilitate migration of lymphocytes into the CNS and induction of inflammatory reactions in the brain.

Downregulated Genes in MS-Derived T-cells - The profile of gene expression in MS-derived T-cells (Figure 4, and Table V) indicates a suppression of apoptosis-related functions in the diseased state. One aspect of failure to induce apoptosis in the MS-derived T cell lines is the significant down-regulation of the gene encoding for the pro-apoptotic molecule **TNF**. A reduction in **TNF** could also contribute to a reduction in the ratio of pro- and anti-apoptotic transcript expression in the anti-MOG T cell lines from MS patients compared to healthy controls. Indeed, inadequate apoptosis present in MS autoreactive T cell lines could lead to insufficient deletion of autoimmune activated T cell clones and increase susceptibility to autoimmunity.

In addition, effectors of MHC class I presentation were revealed to be down-regulated in MS patients' cells. Such down-regulated expression includes the transcript for the **proteasome PA28 complex**, known to be a principal provider of MHC class I-presented peptides in antigen presenting cells, and **HSP70 1A and 1B** variants. **TNF** is also known to stimulate MHC class I presentation in addition to induction of apoptosis. The findings presented herein indicate that a weaker antigenic MHC class I presenting capability might distinguish MS-patient derived T cell lines from their healthy counterparts, and providing powerful diagnostic tools. It is conceivable that a lower expression of MHC class-I on CD4 autoimmune T cells might enable them to escape regulation by CD8 cells that recognize autoimmune idiotypes.

Taken together the combined effects of down-regulation of apoptosis associated genes, up regulation of anti-apoptotic genes, increased expansion capability by autoreactive T cells and enhanced ability to penetrate the CNS may lead to perpetuated pathologic cellular proliferation and tissue destruction within the CNS characteristic of MS, along with increased resistance to

regulation. The specific gene expression profiles described herein can define some of the requirements for an individual to develop MS, and thus have important predictive value, especially in determining MS in the "probable" stage. It is noteworthy that despite activation in vitro with the same MOG epitope, anti-MOG T cells from healthy subjects did not attain the gene expression profile that characterized the MS patient-derived cells. The findings support the concept that not all autoimmune T cells are equal; autoimmune T cells from MS patients follow a unique pattern of T cell activation that appears to be more resilient to apoptosis and can support long term survival. Although T cell lines derived from MS patients and healthy donors responded to the same autoantigen, were both activated T cell populations that proliferated extensively in the presence of IL-2, the gene expression imprints that are unique to each group were preserved. These findings indicate the existence of different T-cell activation mechanisms. The nature of the stimuli that generate aberrant autoimmune T-cell gene expression has yet to be identified in order to determine whether their formation is merely the result of the chronic immune stimulation driven by other factors in MS, or whether such T cells function as primary drivers of the MS process. Characterization of such driver T cells, dictating the state of immunity/autoimmunity can also greatly contribute to understanding autoimmunity and possibly also for designing effective treatments for MS.

TABLES I-V

Table I: Gene Expression Profile from PBMCs of MS vs. Healthy

Identifier	TNOM PValue	Info PValue	t-Test PValue	Log Fold Change	Symbol
U78107	8.55E-11	1.94E-11	4.04E-12	-0.43769	NAPG
M15330	8.55E-11	8.55E-11	2.49E-12	-2.13825	IL1B
X15218	8.55E-11	8.55E-11	1.4E-10	-1.41501	SKI
AF024710	8.55E-11	8.55E-11	1.13E-12	-1.95537	VEGF
U09937	1.84E-09	4.16E-10	2.04E-09	-1.21578	HSUROKR7
AB018343	1.84E-09	4.16E-10	9.05E-12	0.383078	KIAA0800
X74039	1.84E-09	4.16E-10	1.51E-10	-0.67381	PLAUR
M64571	1.84E-09	1.84E-09	2.41E-11	0.416659	MAP4

U64197	1.84E-09	1.84E-09	2.95E-10	-0.62373	SCYA20
X68452	2.57E-08	2.93E-09	9.12E-11	-0.26618	CCND2
AB011161	2.57E-08	2.93E-09	9.64E-11	0.63432	PIP5K1C
L47738	2.57E-08	2.93E-09	7.54E-09	0.31646	PIR121
U78798	2.57E-08	2.93E-09	1.11E-06	-0.3172	TRAF6
M63904	2.57E-08	7.16E-09	5.38E-09	-0.59612	GNA15
U72066	2.57E-08	7.16E-09	4.33E-08	-0.34482	RBBP8
AI184802	2.64E-07	1.61E-08	2.67E-09	-0.21576	HPRP4P
AF077820	2.64E-07	1.61E-08	2.91E-08	0.656852	LRP5
L13740	2.64E-07	1.61E-08	5.83E-08	-1.45891	NR4A1
AL008583	2.64E-07	1.61E-08	1.12E-08	0.250082	
Z24724	2.64E-07	1.61E-08	5.96E-09	-1.10426	
D30783	2.57E-08	2.19E-08	8.95E-10	-1.65011	EREG
U47927	2.57E-08	2.19E-08	5.53E-09	0.545592	USP5
AI560890	2.57E-08	2.19E-08	1.8E-07	0.179028	
Y00630	2.57E-08	3.69E-08	6.65E-09	-2.38485	SERPINB2
N90866	2.64E-07	8.23E-08	2.76E-08	0.304525	CDW52
AF022375	2.64E-07	8.23E-08	1.87E-11	-1.35847	VEGF
M24895	2.11E-06	1.08E-07	1.72E-08	0.476779	AMY2B
AF054176	2.11E-06	1.08E-07	6.47E-09	-0.58138	C1orf7
L20941	2.64E-07	1.08E-07	1.78E-06	-0.58618	FTH1
L05424	2.11E-06	1.08E-07	2.27E-09	-0.58081	HUMSCG19
AB002347	2.11E-06	1.08E-07	7.19E-10	0.371731	KIAA0349
AB023153	2.11E-06	1.08E-07	1.82E-08	0.895842	KIAA0936
AF069517	2.11E-06	1.08E-07	4.91E-07	0.399638	RBM6
X69392	2.64E-07	1.08E-07	1.1E-08	0.297444	RPL26
U51920	2.11E-06	1.08E-07	7.01E-08	-0.28142	SRP54
L22075	2.64E-07	1.71E-07	1.1E-08	-0.55736	GNA13
X04500	2.64E-07	1.71E-07	3.43E-10	-2.12121	IL1B
AB028951	2.64E-07	1.71E-07	8.78E-09	0.543028	KIAA1028
AF004230	2.64E-07	1.71E-07	3.06E-07	0.349166	LILRB1
AF070582	2.64E-07	1.71E-07	3.23E-08	-0.19773	MGC13033
X66363	2.64E-07	1.71E-07	6.53E-07	-0.24505	PCTK1
L33881	2.64E-07	1.71E-07	5.06E-08	-0.59585	PRKCI
U33017	2.64E-07	1.71E-07	5.2E-07	0.373581	SLAM
AJ007042	2.64E-07	1.71E-07	2.1E-07	0.170935	WHSC1
Z93930	2.64E-07	1.71E-07	2.42E-05	-0.39839	XBP1
AF079167	2.64E-07	1.71E-07	7.37E-10	-1.93249	
AF098641	2.64E-07	1.71E-07	1.56E-07	-0.41172	
HG3227-HT3404	2.64E-07	1.71E-07	1.68E-08	-0.25361	
U78302	2.64E-07	1.71E-07	2.41E-08	0.329878	
U91543	2.64E-07	2.49E-07	2.01E-07	0.478678	CHD3
M22919	2.64E-07	2.49E-07	9.52E-08	-0.81053	MYL6
AB029015	2.64E-07	2.49E-07	5.37E-09	0.695063	PLCE2
Z11697	1.37E-05	4.08E-07	3.55E-06	-1.21033	CD83
AL096780	1.37E-05	4.08E-07	2.13E-06	0.34487	CHKL
U51205	1.37E-05	4.08E-07	2.65E-07	-0.76279	COP9
Y08683	1.37E-05	4.08E-07	4.71E-06	0.492738	CPT1B
S52028	2.11E-06	4.08E-07	9.62E-08	-0.81662	CTH
X63368	2.11E-06	4.08E-07	2.3E-08	-0.55432	DNAJB2

M84443	1.37E-05	4.08E-07	4.08E-07	0.303567	GALK2
U32324	1.37E-05	4.08E-07	3.21E-08	0.334966	IL11RA
AB011115	1.37E-05	4.08E-07	3.39E-07	0.382809	KIAA0543
AB014535	1.37E-05	4.08E-07	1.04E-06	0.285282	KIAA0635
X02152	1.37E-05	4.08E-07	4.63E-08	-0.75601	LDHA
AF007130	2.11E-06	4.08E-07	2.51E-06	0.391811	LOC54104
AF007151	1.37E-05	4.08E-07	3.25E-06	0.468343	MMS19L
X82209	2.11E-06	4.08E-07	1.37E-09	-0.45281	MN1
X79882	1.37E-05	4.08E-07	1.78E-07	0.520965	MVP
U91616	1.37E-05	4.08E-07	1.27E-07	-0.80419	NFKBIE
U41815	1.37E-05	4.08E-07	2.16E-07	-0.96931	NUP98
AB011108	1.37E-05	4.08E-07	4.39E-07	0.453498	PRP4
L40377	1.37E-05	4.08E-07	3.49E-07	-0.79409	SERPINB8
X99656	1.37E-05	4.08E-07	1.68E-06	-0.23553	SH3GL1
AJ010059	2.11E-06	4.08E-07	2.95E-06	0.2235	SIT
J02973	1.37E-05	4.08E-07	2.93E-07	-1.30804	THBD
N90862	1.37E-05	4.08E-07	3.28E-08	0.43576	VAMP8
Y14768	1.37E-05	4.08E-07	7.26E-08	0.248383	
U47414	2.11E-06	7.73E-07	2.31E-06	0.370736	CCNG2
AB002386	2.11E-06	7.73E-07	5.34E-09	0.586117	EZH1
U29344	2.11E-06	7.73E-07	2.35E-07	-0.43842	FASN
AF015553	2.11E-06	7.73E-07	2.61E-07	0.61214	GTF2I
AB028981	2.11E-06	7.73E-07	5.34E-07	0.282288	KIAA1058
U29656	2.11E-06	7.73E-07	7.52E-08	0.353186	NME3
X00737	2.11E-06	7.73E-07	5.21E-08	-0.67074	NP
U29185	2.11E-06	7.73E-07	1.56E-07	-1.08006	PRNP
AB007960	2.11E-06	7.73E-07	7.96E-06	0.447772	SH3GLB1
U44839	2.11E-06	7.73E-07	2.54E-07	-0.97008	USP11
U84007	7.44E-05	1.28E-06	0.000235	0.236422	AGL
S78187	7.44E-05	1.28E-06	1.95E-05	0.203265	CDC25B
X82153	7.44E-05	1.28E-06	2.27E-06	0.47844	CTSK
AL050084	7.44E-05	1.28E-06	5.26E-05	0.509331	DC8
X62535	1.37E-05	1.28E-06	5.68E-07	0.243937	DGKA
AB026436	7.44E-05	1.28E-06	0.000219	-0.7589	DUSP10
M98833	7.44E-05	1.28E-06	1.52E-06	0.434288	FLI1
AW051579	1.37E-05	1.28E-06	7.58E-07	0.593476	FLJ10512
X16706	7.44E-05	1.28E-06	1.23E-06	-1.09747	FOSL2
U90917	1.37E-05	1.28E-06	3.89E-07	0.433406	FOXM1
M24194	7.44E-05	1.28E-06	4.38E-06	0.560895	GNB2L1
AJ002190	7.44E-05	1.28E-06	2.17E-08	0.33775	GNPAT
X87949	7.44E-05	1.28E-06	4.05E-07	-0.54468	HSPA5
U96876	7.44E-05	1.28E-06	3.54E-06	-0.45317	INSIG1
AF038564	1.37E-05	1.28E-06	2.05E-07	-0.40446	ITCH
D80011	7.44E-05	1.28E-06	4.2E-07	-0.35073	KIAA0189
AI950382	1.37E-05	1.28E-06	1.63E-07	-0.74128	KIAA0585
AB023235	7.44E-05	1.28E-06	1.43E-05	0.311216	KIAA1018
AB029038	7.44E-05	1.28E-06	7.62E-05	0.364386	KIAA1115
U24166	7.44E-05	1.28E-06	7.52E-06	-0.45293	MAPRE1
X61498	7.44E-05	1.28E-06	8.8E-07	-0.49884	NFKB2
U12767	7.44E-05	1.28E-06	2.84E-07	-1.23483	NR4A3

U85245	7.44E-05	1.28E-06	4.57E-07	0.365266	PIP5K2B
U50928	7.44E-05	1.28E-06	4.72E-06	0.302213	PKD2
U13695	7.44E-05	1.28E-06	1.11E-05	0.805607	PMS1
AA203527	1.37E-05	1.28E-06	1.18E-07	0.281992	RPP20
J02939	7.44E-05	1.28E-06	2.16E-07	-0.87844	SLC3A2
N30151	7.44E-05	1.28E-06	5.05E-05	0.393521	STX16
U52960	2.11E-06	1.28E-06	1.51E-07	-0.84863	SURB7
AF030249	1.37E-05	1.28E-06	1.98E-07	0.534547	
AL022398	7.44E-05	1.28E-06	8.09E-08	0.919627	
HG1103-HT1103	1.37E-05	1.28E-06	1.16E-07	-0.39165	
D30758	2.11E-06	1.8E-06	1.58E-05	0.27738	CENTB1
U75968	2.11E-06	1.8E-06	4.36E-06	0.139542	DDX11
M69199	2.11E-06	1.8E-06	1.45E-07	-1.9021	G0S2
U20982	2.11E-06	1.8E-06	1.2E-08	-0.67125	IGFBP4
AF040707	2.11E-06	1.8E-06	3.57E-07	0.289845	NPR2L
AB007927	2.11E-06	1.8E-06	2.12E-07	0.323787	RERE
AA902713	2.11E-06	1.8E-06	1.44E-06	0.474378	
U66063	2.11E-06	2.24E-06	4.7E-07	0.277185	CAMK2G
D13891	2.11E-06	2.24E-06	4.57E-05	-0.20577	ID2
AL050087	2.11E-06	2.24E-06	1.27E-07	-0.31279	KIAA1785
N23137	2.11E-06	2.24E-06	2.06E-07	0.247311	MPHOSPH9
N42007	2.11E-06	2.24E-06	9.19E-05	0.167986	NUP50
M74525	2.11E-06	2.24E-06	3.5E-07	-0.61792	UBE2B
AF035281	2.11E-06	2.24E-06	4.87E-07	0.472445	
U11732	1.37E-05	3.17E-06	3.04E-07	-0.22574	ETV6
AB002348	1.37E-05	3.17E-06	2.49E-07	0.576346	KIAA0350
AB007891	1.37E-05	3.17E-06	3.99E-05	0.196376	KIAA0431
AI754391	1.37E-05	3.17E-06	1.72E-06	-0.27657	KLF12
D50406	1.37E-05	3.17E-06	2.65E-05	0.461907	RECK
AF070617	1.37E-05	3.17E-06	3.23E-07	0.323494	
M23114	2.11E-06	4.08E-06	1.59E-07	-0.96141	ATP2A2
AF014958	2.11E-06	4.08E-06	1.05E-07	-0.42152	CCRL2
AF067853	1.37E-05	4.31E-06	5.02E-06	0.361707	ADSL
M73547	1.37E-05	4.31E-06	9.2E-08	0.438897	D5S346
W28319	1.37E-05	4.31E-06	1.5E-05	0.294631	FBLN1
AB007895	1.37E-05	4.31E-06	9.61E-07	0.186643	KIAA0435
AB014579	1.37E-05	4.31E-06	6.08E-08	0.367966	MGEA5
AF019083	1.37E-05	4.31E-06	8.34E-07	0.17011	PTENP1
AL080141	1.37E-05	4.31E-06	2.42E-07	0.330868	SEC31B-1
AF110377	1.37E-05	4.31E-06	3.05E-05	0.361232	TRRAP
AB002448	1.37E-05	4.31E-06	2.45E-07	0.468926	
AL049787	1.37E-05	4.31E-06	7.11E-06	0.311278	
U50527	1.37E-05	4.31E-06	5.11E-06	0.416543	
Z32860	1.37E-05	4.31E-06	7.81E-06	0.133192	
AF094481	1.37E-05	5.01E-06	2.74E-07	-0.29045	CGGBP1
U29171	1.37E-05	5.01E-06	1.1E-06	-0.6032	CSNK1D
AL050196	1.37E-05	5.01E-06	2E-05	-0.24688	DKFZP586D2223
U48807	1.37E-05	5.01E-06	4.97E-08	-0.93178	DUSP4
U15552	1.37E-05	5.01E-06	1.67E-05	-0.68094	HSU15552
L13740	1.37E-05	5.01E-06	9.1E-08	-0.61928	NR4A1

AF010309	1.37E-05	5.01E-06	7.36E-07	-0.28533	PIG3
Y18004	1.37E-05	5.01E-06	4.19E-07	-0.9465	SCML2
R90942	1.37E-05	5.01E-06	1.05E-05	-0.17696	ST6GALNACIV
W28612	1.37E-05	5.01E-06	1.7E-06	-0.25519	
X64330	7.44E-05	6.03E-06	2.27E-06	0.297851	ACLY
U49844	7.44E-05	6.03E-06	3.67E-07	0.47168	ATR
AB015019	7.44E-05	6.03E-06	2.75E-07	-0.24515	BAIAP2
AF006513	0.000344	6.03E-06	4.48E-05	-1.45973	CHD1
U56998	0.000344	6.03E-06	3.7E-06	-0.74294	CNK
S68134	0.000344	6.03E-06	8.37E-07	-1.64652	CREM
S68134	0.000344	6.03E-06	4.35E-06	-2.47105	CREM
S68271	0.000344	6.03E-06	3.03E-06	-2.07185	CREM
AF021819	0.000344	6.03E-06	4.41E-05	0.298771	DJ-1
AF029777	1.37E-05	6.03E-06	8.27E-07	0.290159	GCN5L2
U28811	0.000344	6.03E-06	1.33E-06	0.32855	GLG1
S81914	0.000344	6.03E-06	4.18E-07	-1.59146	IER3
X80821	0.000344	6.03E-06	8.51E-05	-0.5606	KIAA0874
L06895	7.44E-05	6.03E-06	1.12E-05	-0.1928	MAD
D78579	1.37E-05	6.03E-06	4.25E-07	-1.65638	NR4A3
D78579	7.44E-05	6.03E-06	9.62E-07	-1.61438	NR4A3
U12767	0.000344	6.03E-06	2.55E-07	-2.13744	NR4A3
M95678	0.000344	6.03E-06	2E-06	0.432923	PLCB2
X51804	0.000344	6.03E-06	7.23E-05	-0.19283	PMI
W28743	0.000344	6.03E-06	2.78E-06	-0.28926	PP1628
X17042	7.44E-05	6.03E-06	6.64E-06	-0.36481	PRG1
M80244	0.000344	6.03E-06	2.72E-06	-0.8522	SLC7A5
AF001294	1.37E-05	6.03E-06	1.23E-06	-0.76359	TSSC3
D49677	7.44E-05	6.03E-06	4.18E-06	0.198707	U2AF1RS2
AB011004	0.000344	6.03E-06	1.41E-06	-1.34073	UAP1
AB011113	1.37E-05	6.03E-06	3.74E-07	0.444795	WDR7
AC002394	0.000344	6.03E-06	0.001473	0.17105	
AL021707	0.000344	6.03E-06	4.95E-06	-2.21462	
AL022398	7.44E-05	6.03E-06	1.1E-07	0.79713	
AL049442	0.000344	6.03E-06	8.09E-06	0.621935	
U17760	0.000344	6.03E-06	4.25E-06	-0.84472	
L22569	1.37E-05	8.66E-06	1.52E-06	0.318129	CTSB
AL031058	1.37E-05	8.66E-06	0.000375	0.149046	DSP
AL080172	1.37E-05	8.66E-06	1.89E-05	0.098968	FLJ21919
M36821	1.37E-05	8.66E-06	2.21E-07	-0.36334	GRO3
U06631	1.37E-05	8.66E-06	1.31E-05	0.486332	H326
L16499	1.37E-05	8.66E-06	5.12E-06	0.374296	HHEX
X53586	1.37E-05	8.66E-06	3.4E-07	0.51291	ITGA6
D87466	1.37E-05	8.66E-06	1.49E-07	0.466046	KIAA0276
N98667	1.37E-05	8.66E-06	3.38E-07	0.367127	KIAA1696
X99142	1.37E-05	8.66E-06	1.24E-06	-0.29773	KRTHB6
AF011333	1.37E-05	8.66E-06	1.55E-05	0.342503	LY75
U70735	1.37E-05	8.66E-06	1.82E-06	0.249185	MOV34-34KD
U02020	1.37E-05	8.66E-06	1.37E-06	-1.13863	PBEF
M31724	1.37E-05	8.66E-06	0.000172	-0.2601	PTPN1
U29175	1.37E-05	8.66E-06	1.9E-06	0.266342	SMARCA4

AL031846	1.37E-05	8.66E-06	0.000418	0.38404	
Y12059	7.44E-05	1.51E-05	5.64E-06	-0.46008	BRD4
U49187	7.44E-05	1.51E-05	1.48E-06	0.671467	C6orf32
X66945	7.44E-05	1.51E-05	1.91E-07	-0.35494	FGFR1
M60922	7.44E-05	1.51E-05	4.47E-08	0.39657	FLOT2
AL049409	7.44E-05	1.51E-05	1.1E-06	0.714173	LEF1
L16794	7.44E-05	1.51E-05	2.23E-05	-0.27553	MEF2D
U77735	7.44E-05	1.51E-05	5.66E-06	0.574142	PIM2
U10117	7.44E-05	1.51E-05	4.07E-06	0.563673	SCYE1
AF023614	1.37E-05	1.51E-05	4.79E-07	-0.20744	TACI
S73591	1.37E-05	1.51E-05	4.68E-06	0.414777	VDUP1
AF052160	7.44E-05	1.51E-05	1.67E-06	0.623021	
L76528	7.44E-05	1.51E-05	6.14E-06	-0.39652	
U51007	7.44E-05	1.51E-05	1.49E-06	0.309996	
D10704	1.37E-05	1.75E-05	4.69E-07	-0.36791	CHK
U97105	1.37E-05	1.75E-05	6.56E-07	1.00615	DPYSL2
U03634	1.37E-05	1.75E-05	1E-06	-0.21467	LBC
L13773	1.37E-05	1.75E-05	6.44E-07	0.247919	MLLT2
M31523	1.37E-05	1.75E-05	2.09E-06	0.36898	TCF3
AL023553	1.37E-05	1.75E-05	2.51E-06	0.226635	
W25984	7.44E-05	2.35E-05	1.42E-05	0.482493	ACTA1
U78521	0.000344	2.35E-05	2.53E-05	0.320909	AIP
M30704	0.000344	2.35E-05	1.65E-05	-0.37795	AREG
X91504	0.001377	2.35E-05	0.00016	0.233217	ARFRP1
U51478	7.44E-05	2.35E-05	6.1E-07	-0.58	ATP1B3
U21551	0.001377	2.35E-05	7.6E-05	-0.3088	BCAT1
AB004066	0.000344	2.35E-05	6.57E-05	-0.60905	BHLHB2
M59040	0.001377	2.35E-05	2.82E-06	-0.46271	CD44
M91670	0.001377	2.35E-05	0.001649	-0.47538	E2-EPF
U43774	0.000344	2.35E-05	8.8E-07	-0.39938	FCAR
AW024285	0.000344	2.35E-05	6.99E-06	-0.42098	FLJ12443
AA780049	7.44E-05	2.35E-05	7.39E-07	0.54912	FLJ21439
AI935146	0.000344	2.35E-05	2.05E-06	-0.46726	GALNT3
AJ011679	0.001377	2.35E-05	4.67E-05	0.243248	GAPCENA
AI670100	7.44E-05	2.35E-05	7.7E-07	0.22677	GRLF1
D87119	7.44E-05	2.35E-05	1.8E-06	0.425625	GS3955
M92432	0.000344	2.35E-05	4.31E-05	0.363033	GUCY2D
D50405	0.001377	2.35E-05	0.000688	0.387926	HDAC1
U07563	7.44E-05	2.35E-05	4.91E-07	-0.25016	HSABLGR3
Y10313	0.001377	2.35E-05	0.003201	-0.35345	IFRD1
D63485	0.000344	2.35E-05	9.04E-05	0.31177	IKKE
L08488	0.000344	2.35E-05	7.54E-06	-0.37883	INPP1
X06256	1.37E-05	2.35E-05	4.89E-07	-0.7357	ITGA5
D42084	0.001377	2.35E-05	7.39E-06	0.222195	KIAA0094
D43947	7.44E-05	2.35E-05	0.000104	0.269941	KIAA0100
AB007870	0.000344	2.35E-05	0.000108	-0.64362	KIAA0410
AI950382	0.000344	2.35E-05	0.000122	-0.65985	KIAA0585
AB014548	7.44E-05	2.35E-05	2.77E-05	0.431229	KIAA0648
AB018297	0.001377	2.35E-05	0.000836	0.195704	KIAA0754
AI970189	0.000344	2.35E-05	6.16E-07	-0.75934	KIAA0997

L04733	0.001377	2.35E-05	8.84E-07	0.306455	KNS2
AF010193	7.44E-05	2.35E-05	1.26E-07	-1.4705	MADH7
U18919	7.44E-05	2.35E-05	1.05E-05	0.271231	NBP
U85430	0.001377	2.35E-05	0.000315	0.317554	NFATC3
S76638	7.44E-05	2.35E-05	7.47E-07	-0.35416	NFKB2
AL050353	0.000344	2.35E-05	4.42E-06	0.179352	OIP2
L20971	0.001377	2.35E-05	0.00089	-0.49725	PDE4B
AF060502	7.44E-05	2.35E-05	0.000114	-0.18239	PEX10
X80497	0.001377	2.35E-05	0.000245	0.313262	PHKA2
AL050371	0.000344	2.35E-05	3.7E-06	0.493288	PISD
U77718	7.44E-05	2.35E-05	6.6E-06	0.352996	PNN
U52427	0.001377	2.35E-05	0.000282	0.329478	POLR2G
U94778	0.000344	2.35E-05	1.18E-05	0.282929	PSTPIP1
U48296	0.001377	2.35E-05	0.00011	-0.89871	PTP4A1
M31166	0.001377	2.35E-05	0.000256	-0.38484	PTX3
AJ001016	7.44E-05	2.35E-05	1.08E-05	-0.28245	RAMP3
AF040965	0.001377	2.35E-05	0.001101	-0.38591	RES4-25
J04130	0.000344	2.35E-05	3.02E-06	-0.62071	SCYA4
U81800	0.000344	2.35E-05	4.28E-05	-0.49523	SLC16A3
AB000734	0.001377	2.35E-05	0.000883	-0.58764	SSI-1
U38847	7.44E-05	2.35E-05	9.91E-07	0.222946	TARBP1
M63180	0.001377	2.35E-05	1.03E-05	-0.33301	TARS
D15050	0.001377	2.35E-05	0.000192	-1.12874	TCF8
M12959	7.44E-05	2.35E-05	1.61E-06	0.128482	TRA@
X00734	0.001377	2.35E-05	0.000384	-0.34516	TUBB5
AJ001340	0.001377	2.35E-05	4.21E-05	0.181208	U3-55K
Y08614	0.001377	2.35E-05	6.92E-05	0.305659	XPO1
AF054589	0.000344	2.35E-05	1.98E-06	0.945394	
AL022398	7.44E-05	2.35E-05	2.4E-06	0.493166	
AL031178	7.44E-05	2.35E-05	3.18E-05	0.410068	
AL049782	7.44E-05	2.35E-05	7.66E-07	0.237794	
HG1471-HT3923	0.001377	2.35E-05	0.000519	0.203133	
HG4582-HT4987	7.44E-05	2.35E-05	4.63E-07	-0.39588	
U96629	0.001377	2.35E-05	1E-04	0.277256	
D64110	7.44E-05	2.58E-05	7.49E-05	-0.51036	BTG3
J04111	7.44E-05	2.58E-05	0.000108	-1.60276	JUN
J04111	7.44E-05	2.58E-05	4.68E-05	-1.14014	JUN
X56681	7.44E-05	2.58E-05	0.000112	-0.48711	JUND
D21853	7.44E-05	2.58E-05	0.000403	-0.25594	KIAA0111
X80692	7.44E-05	2.58E-05	3.44E-05	-1.1939	MAPK6
S76638	7.44E-05	2.58E-05	5.23E-05	-0.46026	NFKB2
U65785	7.44E-05	2.58E-05	9.67E-06	-0.2389	ORP150
AB016247	7.44E-05	2.58E-05	3.13E-05	-0.57287	SC5DL
M55153	7.44E-05	2.58E-05	4.77E-06	-0.27465	TGM2
U02570	1.37E-05	2.81E-05	1.26E-06	0.432431	ARHGAP1
X04366	1.37E-05	2.81E-05	5.11E-06	0.346076	CAPN1
L10413	1.37E-05	2.81E-05	6.46E-06	0.207231	FNTA
AF055001	1.37E-05	2.81E-05	9.78E-06	-0.9457	HERPUD1
AI523538	1.37E-05	2.81E-05	0.004471	-0.1584	HIPK3
X59373	1.37E-05	2.81E-05	1.31E-05	-0.22992	HOXD10

X99209	1.37E-05	2.81E-05	2.65E-05	0.239777	HRMT1L1
M65217	1.37E-05	2.81E-05	1.02E-05	0.33377	HSF2
X17025	1.37E-05	2.81E-05	1.45E-05	-0.44351	IDI1
M35878	1.37E-05	2.81E-05	4.29E-05	-0.25267	IGFBP3
D63486	1.37E-05	2.81E-05	9.69E-06	0.235319	KIAA0152
AB002303	1.37E-05	2.81E-05	1.86E-05	-0.39642	KIAA0305
U20816	1.37E-05	2.81E-05	4.92E-05	-0.20145	NFKB2
M61906	1.37E-05	2.81E-05	5.93E-06	-0.39875	PIK3R1
U13695	1.37E-05	2.81E-05	1.31E-05	0.362255	PMS1
U38979	1.37E-05	2.81E-05	3.95E-05	0.158105	PMS2L9
X70218	1.37E-05	2.81E-05	2.44E-06	-0.74691	PPP4C
AC002400	1.37E-05	2.81E-05	2.28E-06	-0.25834	
AC005390	1.37E-05	2.81E-05	2.99E-05	-0.24231	
AF070606	1.37E-05	2.81E-05	1.48E-06	-0.89337	
HG2724-HT2820	1.37E-05	2.81E-05	5.17E-06	-1.33814	
X84194	7.44E-05	4.67E-05	6.38E-05	0.23578	ACYP1
AF039656	0.00482	4.67E-05	0.000251	-0.73273	BASP1
AB002384	0.00482	4.67E-05	4.22E-05	0.548091	C6orf32
X98172	7.44E-05	4.67E-05	5.29E-07	0.507556	CASP8
U60521	7.44E-05	4.67E-05	8.13E-06	-0.36762	CASP9
U11791	0.00482	4.67E-05	0.000363	-1.0232	CCNH
U67615	0.00482	4.67E-05	0.000948	1.23433	CHS1
AF037339	0.000344	4.67E-05	1.59E-05	-0.33549	CLPTM1
U65928	7.44E-05	4.67E-05	2.85E-07	0.408918	COPS5
U37408	7.44E-05	4.67E-05	3.06E-05	0.157458	CTBP1
AB023143	0.00482	4.67E-05	0.001982	0.215415	DEFCAP
AB014888	0.001377	4.67E-05	0.000204	-0.34841	DNAJB6
M60278	0.00482	4.67E-05	3.33E-05	-0.9007	DTR
U88629	0.000344	4.67E-05	9.58E-07	-0.32607	ELL2
M31899	0.000344	4.67E-05	0.000339	0.274507	ERCC3
M94856	7.44E-05	4.67E-05	4.99E-06	-0.23847	FABP5
X86779	0.001377	4.67E-05	1.08E-05	0.140032	FASTK
L00634	0.00482	4.67E-05	0.00019	0.205256	FNTA
AF078077	0.000344	4.67E-05	1.44E-05	-1.47649	GADD45B
D87119	7.44E-05	4.67E-05	4.62E-06	0.557116	GS3955
X17644	7.44E-05	4.67E-05	6.72E-06	-0.71963	GSPT1
L19314	0.00482	4.67E-05	0.000922	-0.35113	HRY
U05681	7.44E-05	4.67E-05	3.37E-06	-0.35383	HSBCL3S2
J00139	0.00482	4.67E-05	0.000196	-0.12797	HUMFOL5
M24283	0.000344	4.67E-05	3.71E-06	-1.32611	ICAM1
M62403	7.44E-05	4.67E-05	5.57E-07	-0.53749	IGFBP4
M28130	7.44E-05	4.67E-05	8.02E-07	-2.27292	IL8
Z56281	0.001377	4.67E-05	0.000243	0.309173	IRF3
L12002	7.44E-05	4.67E-05	1.23E-06	0.286717	ITGA4
K00558	0.001377	4.67E-05	0.002498	0.12909	K-ALPHA-1
AL044599	0.001377	4.67E-05	8.81E-05	0.321294	KIAA0222
AB002344	0.000344	4.67E-05	1.04E-05	-0.39307	KIAA0346
AB007889	7.44E-05	4.67E-05	2.33E-05	0.255643	KIAA0429
AB007916	0.00482	4.67E-05	0.000147	0.493018	KIAA0447
AB014538	0.000344	4.67E-05	1.98E-06	-0.63923	KIAA0638

AF055004	7.44E-05	4.67E-05	9.29E-05	0.200537	KIAA0763
AI148772	0.000344	4.67E-05	4.18E-06	-1.02619	KYNU
AF064491	0.00482	4.67E-05	0.000148	-0.54215	LDB1
L78132	7.44E-05	4.67E-05	5.15E-07	0.358576	LGALS8
X83441	7.44E-05	4.67E-05	6.75E-06	-0.17796	LIG4
AF055581	7.44E-05	4.67E-05	5.69E-06	-1.05728	LNK
AL049963	0.000344	4.67E-05	8.36E-07	-0.74421	LOC64116
AF014837	0.00482	4.67E-05	0.000636	0.325349	M6A
D14497	0.001377	4.67E-05	3.68E-05	-0.58619	MAP3K8
X75346	7.44E-05	4.67E-05	1.99E-05	-0.37877	MAPKAPK2
M62324	0.001377	4.67E-05	5.46E-05	-0.44552	MRF-1
AB023208	0.000344	4.67E-05	1.37E-05	0.293901	MSF
AF072928	0.001377	4.67E-05	1.13E-05	-0.3089	MTMR6
AF045451	0.000344	4.67E-05	6.34E-06	-0.40149	NAB1
M58603	7.44E-05	4.67E-05	1.28E-06	-0.73537	NFKB1
U07132	0.00482	4.67E-05	0.001821	-0.14679	NR1H2
X75918	7.44E-05	4.67E-05	3.5E-05	-1.61126	NR4A2
S77154	0.00482	4.67E-05	0.000304	-1.33785	NR4A2
AB020657	0.00482	4.67E-05	2.75E-05	-0.50544	NS1-BP
D88674	7.44E-05	4.67E-05	6.26E-06	-0.99818	OAZIN
U27459	0.00482	4.67E-05	3.39E-05	0.430016	ORC2L
AF000545	7.44E-05	4.67E-05	3.48E-06	-0.85393	P2Y10
AF005043	7.44E-05	4.67E-05	2.7E-06	0.408592	PARG
AF026086	0.000344	4.67E-05	2.66E-06	0.297942	PEX1
AJ001625	7.44E-05	4.67E-05	9.91E-05	0.36837	PEX3
U30255	0.001377	4.67E-05	0.000826	0.325906	PGD
M61906	0.000344	4.67E-05	0.000611	-0.2492	PIK3R1
M60483	0.000344	4.67E-05	3.17E-05	-0.32565	PPP2CA
U14603	7.44E-05	4.67E-05	4.46E-05	0.427268	PTP4A2
AF069517	0.001377	4.67E-05	0.000441	0.330897	RBM6
M83221	0.000344	4.67E-05	1.58E-05	-0.26782	RELB
AF037195	0.00482	4.67E-05	8.27E-05	0.959619	RGS14
L07597	0.00482	4.67E-05	0.000169	0.277243	RPS6KA1
X15217	7.44E-05	4.67E-05	3.77E-07	-0.2371	SKIL
M20681	0.001377	4.67E-05	1.92E-05	-0.99917	SLC2A3
AF030409	7.44E-05	4.67E-05	7.66E-06	0.412043	SLC9A6
AJ224358	0.00482	4.67E-05	0.009613	0.14432	SURF5
U49928	0.000344	4.67E-05	6.31E-06	0.352648	TAB1
X89750	7.44E-05	4.67E-05	7.38E-06	-1.51687	TGIF
AA453183	0.001377	4.67E-05	4.48E-05	-0.61646	TIM17
M31165	7.44E-05	4.67E-05	1.38E-06	-0.34617	TNFAIP6
AF064090	0.001377	4.67E-05	4.05E-05	-0.38921	TNFSF14
AF082557	0.001377	4.67E-05	2.23E-06	0.226994	TNKS
D87448	0.00482	4.67E-05	0.000735	0.468196	TOPBP1
X05276	0.00482	4.67E-05	8.97E-05	-0.50457	TPM4
D50919	0.00482	4.67E-05	4.02E-05	0.332326	TRIM14
J03258	0.00482	4.67E-05	8.78E-05	-0.33021	VDR
AB007973	0.00482	4.67E-05	0.000146	0.271053	
AF041081	0.00482	4.67E-05	5.92E-05	0.26539	
AI889718	7.44E-05	4.67E-05	0.000143	-0.15002	

AL021154	0.000344	4.67E-05	2.19E-06	-0.82935	
AL049340	0.000344	4.67E-05	4.87E-05	-0.91769	
AL050078	0.000344	4.67E-05	1.63E-05	-0.2875	
AL050378	0.000344	4.67E-05	5.72E-06	0.360577	
D50525	0.000344	4.67E-05	3.02E-06	0.486698	
J04755	7.44E-05	4.67E-05	6.75E-05	-0.37296	
M60784	7.44E-05	4.67E-05	1.24E-06	0.559903	
M63978	0.000344	4.67E-05	1.77E-06	-0.44762	
U90909	0.00482	4.67E-05	3.74E-05	-0.64272	
X63547	0.001377	4.67E-05	0.000303	0.505712	
AA135683	0.000344	5.23E-05	0.000289	-0.69258	BASP1
S78771	0.000344	5.23E-05	2.55E-06	-0.31389	BRD2
AL080156	0.000344	5.23E-05	3.52E-05	-0.94419	DKFZP434J214
D14838	0.000344	5.23E-05	7.34E-06	-0.50648	FGF9
W28281	0.000344	5.23E-05	8.96E-06	-1.09149	GABARAPL1
AB002344	7.44E-05	5.23E-05	8.48E-07	-1.00068	KIAA0346
U23070	0.000344	5.23E-05	3.62E-05	-0.12321	NMA
U04636	0.000344	5.23E-05	2.81E-06	-1.85123	PTGS2
U47634	0.000344	5.23E-05	0.002405	-0.21686	TUBB4
S73149	0.000344	5.23E-05	0.003714	-0.15741	
M63256	0.000344	5.92E-05	6.54E-07	0.454561	CDR2
U94905	0.000344	5.92E-05	2.08E-05	0.388608	DGKZ
AF012023	7.44E-05	5.92E-05	1.02E-06	0.50623	ICAP-1A
L10717	0.000344	5.92E-05	0.000158	0.345558	ITK
D29642	0.000344	5.92E-05	8.3E-06	0.327019	KIAA0053
AB011128	0.000344	5.92E-05	0.000584	0.151161	KIAA0556
AF075587	0.000344	5.92E-05	7.55E-06	0.4405	KIAA0916
U66464	0.000344	5.92E-05	2.93E-05	0.255675	MAP4K1
U18919	0.000344	5.92E-05	0.000573	0.277847	NBP
X58965	0.000344	5.92E-05	7.34E-05	0.231912	NME2
X13403	7.44E-05	5.92E-05	4.21E-07	0.146032	POU2F1
D89859	0.000344	5.92E-05	1.56E-05	0.375402	ZFP161
AF052100	0.000344	5.92E-05	1.37E-05	0.290021	
N53547	7.44E-05	7.24E-05	1.8E-07	0.296678	MGC5508
L35013	0.000344	7.24E-05	0.000112	-0.17331	SF3B4
Y17829	7.44E-05	7.24E-05	5.49E-06	-0.6508	SYN47
AL049987	7.44E-05	7.24E-05	2.39E-05	0.193082	
X66436	0.000344	7.24E-05	1.88E-06	-0.26662	
Z80345	7.44E-05	9.64E-05	7.31E-06	0.412137	ACADS
U27467	7.44E-05	9.64E-05	5.65E-06	-0.56637	BCL2A1
AI961669	7.44E-05	9.64E-05	0.000107	-0.1656	BIG2
X61123	7.44E-05	9.64E-05	4.17E-07	-1.15256	BTG1
U49187	7.44E-05	9.64E-05	3.53E-06	0.511392	C6orf32
D13639	7.44E-05	9.64E-05	8.56E-06	-0.64255	CCND2
AL035398	7.44E-05	9.64E-05	0.000153	0.353395	CGI-51
U15932	7.44E-05	9.64E-05	0.00031	-1.26603	DUSP5
AD001530	7.44E-05	9.64E-05	3.06E-05	-0.37019	DXS9928E
Y07909	7.44E-05	9.64E-05	0.000161	-0.23489	EMP1
W27152	7.44E-05	9.64E-05	0.000502	0.186359	FLJ10569
L17131	7.44E-05	9.64E-05	1.48E-05	-0.24039	HMGIY

X04430	7.44E-05	9.64E-05	4.15E-05	-0.21816	IL6
AB014608	7.44E-05	9.64E-05	4.59E-06	0.41494	KIAA0708
AF061258	7.44E-05	9.64E-05	1.58E-06	0.622201	LIM
U90919	7.44E-05	9.64E-05	7.23E-06	-0.50014	LOC57862
J05037	7.44E-05	9.64E-05	0.000185	-0.19243	SDS
X70944	7.44E-05	9.64E-05	2.08E-05	-0.72892	SFPQ
L41887	7.44E-05	9.64E-05	6.74E-06	-0.52203	SFRS7
X59871	7.44E-05	9.64E-05	1.91E-05	0.376648	TCF7
AI742846	7.44E-05	9.64E-05	0.000374	-0.48069	VAPA
HG2007-HT2056	7.44E-05	9.64E-05	4.01E-06	-0.41408	
X58141	7.44E-05	9.64E-05	1.75E-06	0.384254	
AB018323	7.44E-05	0.000106	2.41E-05	0.432301	GASC1
AB023192	7.44E-05	0.000106	0.000138	0.196185	I-1
AB020638	7.44E-05	0.000106	5.26E-05	0.233629	KIAA0831
U49395	7.44E-05	0.000106	0.001916	0.169175	P2RX5
M23379	7.44E-05	0.000106	3.22E-05	0.42571	RASA1
AF034176	7.44E-05	0.000106	0.000333	0.332105	
AJ012755	7.44E-05	0.000106	0.000296	0.26445	
AB007934	7.44E-05	0.000119	6.08E-06	0.345799	ACF7
M80899	7.44E-05	0.000119	2.48E-05	0.419409	AHNAK
AB014529	7.44E-05	0.000119	1.84E-05	0.43403	AKAP11
U37547	7.44E-05	0.000119	6.74E-06	-0.71736	BIRC2
U72649	7.44E-05	0.000119	0.000207	-0.30079	BTG2
D49738	7.44E-05	0.000119	0.000136	0.292742	CKAP1
AJ006267	7.44E-05	0.000119	7.19E-06	0.427023	CLPX
W28167	7.44E-05	0.000119	1.16E-05	0.214921	COPS7A
U18300	7.44E-05	0.000119	2.43E-06	0.183171	DDB2
AI133727	7.44E-05	0.000119	1.43E-06	0.181464	FLB6421
AA526812	7.44E-05	0.000119	0.000106	0.259476	FLJ10326
D64142	7.44E-05	0.000119	1.66E-05	0.528036	H1FX
U60319	7.44E-05	0.000119	0.001064	0.194324	HFE
M17017	7.44E-05	0.000119	1.43E-06	-1.74073	IL8
D32053	7.44E-05	0.000119	0.003279	0.222661	KARS
AB007914	7.44E-05	0.000119	7.13E-05	0.302838	KIAA0445
U10485	7.44E-05	0.000119	7.4E-06	0.270352	LRMP
U29656	7.44E-05	0.000119	4.31E-06	0.471876	NME3
AB014604	7.44E-05	0.000119	1.72E-05	0.425787	OSBPL3
U41745	7.44E-05	0.000119	0.00204	0.230274	PDAP1
S90469	7.44E-05	0.000119	5.56E-06	-0.2636	POR
M26683	7.44E-05	0.000119	3.7E-06	-0.16179	SCYA2
X81789	7.44E-05	0.000119	2.23E-05	0.143079	SF3A3
L14595	7.44E-05	0.000119	3.55E-05	-0.1953	SLC1A4
AL079286	7.44E-05	0.000119	0.000245	0.165851	STAU2
AA845349	7.44E-05	0.000119	7.78E-07	0.457176	TRIP7
X59303	7.44E-05	0.000119	0.000124	0.224891	VARS2
AB023219	7.44E-05	0.000119	1.41E-05	0.316475	
M58603	7.44E-05	0.000129	9.08E-06	-0.56835	NFKB1
X77723	7.44E-05	0.000129	0.006788	-0.24317	RAB5EP
AF117829	7.44E-05	0.000129	2.61E-06	-0.57516	RIPK2
U52960	7.44E-05	0.000129	0.001042	-0.24648	SURB7

U84011	0.00482	0.000149	0.000134	0.286331	AGL
U90552	0.000344	0.000149	0.000182	0.288509	BTN3A1
M16336	0.00482	0.000149	0.000224	0.218007	CD2
U03106	0.000344	0.000149	0.000252	-0.87784	CDKN1A
AB009285	0.001377	0.000149	0.000137	0.235726	CFDP1
U63289	0.001377	0.000149	0.001722	-0.43517	CUGBP1
AF000430	0.00482	0.000149	0.000694	-0.19887	DNM1L
L11329	0.001377	0.000149	0.000142	-0.56584	DUSP2
AB007619	0.00482	0.000149	0.002073	0.198391	EBAG9
X81625	0.00482	0.000149	6.92E-05	-0.80689	ETF1
AL050128	0.000344	0.000149	1.81E-05	0.459416	FAM8A1
L49169	0.001377	0.000149	8.18E-05	-2.09549	FOSB
L25665	0.000344	0.000149	3.34E-06	-0.4513	GNL1
AI494623	0.00482	0.000149	0.000304	0.187206	HCDI
D89678	0.001377	0.000149	3.03E-05	0.197298	HNRPDL
U07563	0.000344	0.000149	1.02E-05	-0.23627	HSABLGR3
W28589	0.00482	0.000149	0.000129	0.170457	HSPD1
N29665	0.000344	0.000149	3.34E-05	0.593294	KIAA0618
AB023207	0.000344	0.000149	8.64E-06	-0.4056	KIAA0990
AL079277	0.00482	0.000149	0.000161	0.200656	LOC54103
Z14138	0.001377	0.000149	0.000197	-0.85008	MAP3K8
N23137	0.001377	0.000149	4.12E-06	0.244083	MPHOSPH9
AF050640	0.001377	0.000149	6.03E-05	0.324021	NDUFS2
AF069987	0.001377	0.000149	4.44E-05	0.203382	NIT1
AF043325	0.000344	0.000149	1.06E-05	0.328186	NMT2
M10901	0.001377	0.000149	1.91E-05	-0.58982	NR3C1
M12267	0.000344	0.000149	4.07E-06	-0.3279	OAT
U02882	0.00482	0.000149	0.000223	-0.99878	PDE4D
AF059531	0.000344	0.000149	6.73E-06	0.546441	PRMT3
M29893	0.001377	0.000149	9.96E-05	-0.15688	RALA
AB029028	0.001377	0.000149	9.11E-06	0.482258	RAP140
AB007448	0.00482	0.000149	0.000777	-0.319	SLC22A4
D87969	0.00482	0.000149	0.001578	0.401991	SLC35A1
U66615	0.00482	0.000149	0.000196	0.235993	SMARCC1
U46691	0.00482	0.000149	1.48E-05	-0.85179	SUPT6H
AF049910	0.00482	0.000149	0.000373	-0.32787	TACC1
X14787	0.001377	0.000149	2.88E-05	-0.19161	THBS1
AI375913	0.00482	0.000149	0.000905	-0.12102	TOP2A
X02344	0.001377	0.000149	0.00414	-0.20405	TUBB2
AF104421	0.000344	0.000149	6.5E-06	0.349373	UROD
J03258	0.000344	0.000149	1.21E-06	-0.58295	VDR
M58297	0.000344	0.000149	1.57E-05	0.185829	ZNF42
Y11681	0.000344	0.000149	1.92E-05	0.234481	
AF104942	0.001377	0.00019	4.83E-05	0.464438	ABCC5
L07261	0.000344	0.00019	0.003564	0.29763	ADD1
L19871	0.001377	0.00019	0.000105	-0.19867	ATF3
J04027	0.000344	0.00019	0.000133	-0.42466	ATP2B1
M83363	0.001377	0.00019	0.004471	0.177565	ATP2B4
AF038195	0.000344	0.00019	0.000134	0.281425	BCS1L
S78771	0.001377	0.00019	0.000145	-0.24109	BRD2

L07044	0.001377	0.00019	0.000284	0.186013	CAMK2G
M28170	0.000344	0.00019	2.96E-05	0.356602	CD19
Y08682	0.000344	0.00019	0.000118	0.17398	CPT1B
AF046059	0.001377	0.00019	0.000665	0.204072	CREME9
L06797	0.001377	0.00019	0.000455	-0.93505	CXCR4
L39874	0.000344	0.00019	0.000354	0.353702	DCTD
AC004475	0.000344	0.00019	2.86E-05	0.25205	DKFZP434E2216
AI538172	0.001377	0.00019	0.000621	0.243057	DKFZp761B2423
AF010187	0.000344	0.00019	1E-05	0.361895	FIBP
AW051579	0.000344	0.00019	0.000258	0.390285	FLJ10512
M22632	0.001377	0.00019	1.34E-05	0.157239	GOT2
X59372	0.001377	0.00019	0.000528	-0.12959	HOXD9
X12433	0.000344	0.00019	1.07E-05	-0.39946	HS1-2
X15183	0.000344	0.00019	0.000645	-0.22973	HSPCA
AI912041	0.001377	0.00019	5.21E-05	-0.38517	HSPE1
X75315	0.000344	0.00019	0.010841	-0.64335	HSRNASEB
L42324	0.000344	0.00019	0.000262	-0.31758	HUMFRCG
X69433	0.001377	0.00019	0.002925	0.209735	IDH2
Y00093	0.000344	0.00019	2.6E-05	-0.39318	ITGAX
M88458	0.001377	0.00019	0.002031	-0.15998	KDELR2
AB011114	0.000344	0.00019	3.13E-05	0.278271	KIAA0542
AB011135	0.000344	0.00019	0.000149	0.247752	KIAA0563
U57721	0.001377	0.00019	3.47E-05	-0.23188	KYNU
Y11395	0.001377	0.00019	8.58E-05	0.34059	LANCL1
AI652660	0.000344	0.00019	2.28E-05	0.385107	LOC51112
AB026118	0.001377	0.00019	4.47E-06	-0.24886	MALT1
AB011144	0.000344	0.00019	9.36E-05	0.26851	MCM3AP
AI620381	0.000344	0.00019	8.06E-06	0.29605	MGC3077
AI525633	0.000344	0.00019	2.44E-05	0.170916	MGC5576
X16396	0.000344	0.00019	3.27E-06	-0.6151	MTHFD2
V00568	0.000344	0.00019	0.000769	0.549224	MYC
AL050281	0.000344	0.00019	2.85E-06	0.30517	NAG
AI985272	0.000344	0.00019	0.000474	-0.2571	NMB
D38524	0.000344	0.00019	0.001313	0.228851	NT5B
AJ225089	0.000344	0.00019	0.000531	-0.2589	OASL
Z82200	0.000344	0.00019	0.000136	-0.28579	P2Y10
X63564	0.001377	0.00019	1.7E-05	-0.28202	POLR2A
S57501	0.001377	0.00019	0.002179	0.267744	PPP1CA
X07109	0.000344	0.00019	0.000694	0.167774	PRKCB1
M28209	0.000344	0.00019	0.000392	-0.52456	RAB1
M87339	0.000344	0.00019	3.41E-05	0.248151	RFC4
Z14000	0.000344	0.00019	3.91E-06	-0.33734	RING1
X06815	0.000344	0.00019	3.5E-05	0.293968	SNRP70
L23959	0.000344	0.00019	1.82E-05	-0.36834	TFDP1
AB018262	0.000344	0.00019	0.000241	0.319056	TOMM70A
X00437	0.001377	0.00019	0.00022	0.248344	TRB@
AF061016	0.000344	0.00019	0.000264	0.349913	UGDH
U62392	0.000344	0.00019	2.74E-05	-0.65983	ZNF193
X78925	0.001377	0.00019	0.001253	-0.28003	ZNF267
AI655015	0.001377	0.00019	0.00444	0.74681	

AL049387	0.001377	0.00019	5.12E-06	0.379296	
AL050376	0.000344	0.00019	0.00026	0.410405	
AB008775	0.000344	0.000304	1.88E-06	-0.80745	AQP9
AI141670	0.000344	0.000304	1.6E-06	-0.2494	CLCN2
AL080071	0.000344	0.000304	3.12E-06	0.237367	DKFZP564M082
AB028964	0.000344	0.000304	5.07E-05	0.351352	KIAA1041
M16801	0.001377	0.000304	0.000458	0.412733	NR3C2
N36842	0.001377	0.000304	0.000577	0.172944	UPF3A
AL096752	0.000344	0.000304	0.000323	-0.20419	
U76421	0.000344	0.000402	0.000278	0.226301	ADARB1
L13939	0.001377	0.000402	0.000215	0.180874	AP1B1
X97074	0.001377	0.000402	0.001924	0.298218	AP2S1
U72936	0.000344	0.000402	1.03E-05	0.356824	ATRX
X94910	0.000344	0.000402	0.000204	0.249294	C12orf8
U18291	0.000344	0.000402	2.45E-05	0.594377	CDC16
L22005	0.001377	0.000402	0.000111	-0.15257	CDC34
M59287	0.00482	0.000402	0.000276	-0.72279	CLK1
U25435	0.000344	0.000402	0.000648	0.264876	CTCF
L39874	0.000344	0.000402	2.41E-05	0.211923	DCTD
X52104	0.000344	0.000402	0.000159	0.317963	DDX5
AL050062	0.000344	0.000402	0.000377	0.36401	DKFZP566K023
AL080081	0.00482	0.000402	0.000103	-0.60871	DNAJB9
X63741	0.001377	0.000402	0.000175	-0.59207	EGR3
D13988	0.001377	0.000402	0.000371	0.14676	GDI2
M27492	0.000344	0.000402	2.01E-06	-0.32619	IL1R1
S66213	0.000344	0.000402	9.56E-05	0.247863	ITGA6
AJ005896	0.000344	0.000402	5.38E-05	0.210462	JM4
Y10745	0.00482	0.000402	6.39E-05	-0.30524	KCNJ15
AB002374	0.00482	0.000402	0.000916	0.20284	KIAA0376
AB007874	0.001377	0.000402	0.000181	-0.21662	KIAA0414
AB011133	0.00482	0.000402	0.000521	0.302843	KIAA0561
AB018335	0.00482	0.000402	9.03E-05	0.234274	KIAA0792
M13452	0.00482	0.000402	0.00148	-0.28339	LMNA
X68836	0.00482	0.000402	2.15E-05	-0.57967	MAT2A
U79256	0.000344	0.000402	2.24E-05	0.328028	MGC14258
X76538	0.001377	0.000402	5.62E-05	0.408464	MPV17
AB011093	0.000344	0.000402	0.000101	0.612928	P114-RHO-GEF
X66363	0.001377	0.000402	6.8E-05	-0.24041	PCTK1
U13695	0.00482	0.000402	2.31E-05	0.31531	PMS1
D87078	0.000344	0.000402	3.88E-05	0.497225	PUM2
Z97074	0.001377	0.000402	3.97E-05	0.296662	RAB9P40
X90530	0.000344	0.000402	3.52E-05	0.254197	RAGB
U75679	0.001377	0.000402	0.000139	-0.29594	SLBP
AF007142	0.000344	0.000402	3.15E-06	0.678734	
AL021977	0.00482	0.000402	8.82E-05	-0.82538	
AL080192	0.001377	0.000402	4.26E-05	0.201319	
HG1980-HT2023	0.00482	0.000402	0.003775	-0.48359	
U47924	0.001377	0.000402	0.000134	0.52195	
U83661	0.000344	0.000444	9.97E-06	0.270218	ABCC5
AI961929	0.000344	0.000444	1.88E-05	0.461528	ARHGAP1

X78817	0.000344	0.000444	2.82E-05	0.281835	ARHGAP4
AL080164	0.000344	0.000444	0.000218	0.268161	DKFZP564C1940
X90392	0.000344	0.000444	0.000208	0.150242	DNASE1L1
AI561196	0.000344	0.000444	0.000156	0.302434	FLJ11806
AJ008112	0.000344	0.000444	0.000246	-0.32126	FMNL
M94630	0.000344	0.000444	0.000244	0.274532	HNRPD
M38180	0.000344	0.000444	0.003037	-0.15741	HSD3B1
U79274	0.000344	0.000444	9.67E-05	0.285563	HSU79274
AB014585	0.000344	0.000444	6.48E-05	0.460196	KIAA0685
AB029001	0.000344	0.000444	0.000183	-0.33324	KIAA1078
AA045160	0.000344	0.000444	4.62E-05	0.179556	MRPS14
M96824	0.000344	0.000444	2.18E-05	0.139326	NUCB1
Y10055	0.000344	0.000444	9.91E-06	0.176067	PIK3CD
Z54367	0.000344	0.000444	1.3E-05	-0.39738	PLEC1
AF014402	0.000344	0.000444	7.63E-05	0.147061	PPAP2A
M30773	0.000344	0.000444	0.001161	0.41229	PPP3R1
M29386	0.000344	0.000444	6.26E-05	-0.23554	PRL
X02910	0.000344	0.000444	0.001378	-0.17579	TNF
S76792	0.000344	0.000444	0.000211	-0.16737	TNFRSF4
Y09008	0.000344	0.000444	0.000352	0.168444	UNG
U18009	0.000344	0.000444	0.002896	0.204706	VATI
D14533	0.000344	0.000444	0.000837	0.246085	XPA
W27419	0.000344	0.000444	2.83E-05	-0.44121	
Z85986	0.000344	0.000444	0.000407	-0.2149	
Z99716	0.000344	0.000444	5.14E-05	0.324642	
U50939	0.001377	0.000525	1.19E-05	0.235552	APPBP1
Y15521	0.00482	0.000525	0.000492	-0.28889	ASMTL
J05682	0.00482	0.000525	0.000291	-0.33004	ATP6C
D26362	0.00482	0.000525	0.000707	0.247252	BRD3
AL120687	0.001377	0.000525	1.21E-05	-0.55731	CSH1
U20350	0.00482	0.000525	0.010386	0.383475	CX3CR1
X04011	0.00482	0.000525	0.000154	0.348439	CYBB
U78524	0.001377	0.000525	6.56E-05	-0.36872	DDXBP1
U87947	0.001377	0.000525	5.05E-05	-0.29673	EMP3
AL035252	0.00482	0.000525	0.003735	0.074075	ENTPD6
X04828	0.00482	0.000525	0.0015	0.256297	GNAI2
X56841	0.001377	0.000525	4.37E-05	0.338907	HLA-E
D49410	0.00482	0.000525	0.00016	-0.21753	HUMIL3RA12
L40586	0.00482	0.000525	3.02E-05	-0.20891	IDS
X52015	0.00482	0.000525	0.00032	-0.54051	IL1RN
D31888	0.00482	0.000525	7.5E-06	-0.44687	KIAA0071
D42047	0.001377	0.000525	3.5E-05	0.226884	KIAA0089
AB007958	0.00482	0.000525	0.00023	0.259725	KIAA0489
AB011100	0.00482	0.000525	0.000193	0.418151	KIAA0528
AB014553	0.00482	0.000525	0.002002	-0.25439	KIAA0653
AI888084	0.001377	0.000525	3.57E-05	0.391754	KIAA1624
X61118	0.00482	0.000525	0.001631	0.292879	LMO2
AJ004832	0.00482	0.000525	0.001715	0.30393	NTE
AB020631	0.001377	0.000525	0.000212	0.379354	PCF11
AB002359	0.00482	0.000525	2.36E-05	0.271468	PFAS

AB012229	0.001377	0.000525	0.000168	-0.59579	PFKFB3
M83088	0.001377	0.000525	3.5E-05	0.439367	PGM1
X84908	0.001377	0.000525	2.25E-05	0.331887	PHKB
U48250	0.001377	0.000525	8.51E-05	-0.2234	PRKCBP2
AB007851	0.000344	0.000525	1.95E-05	0.481768	PRPSAP2
X97267	0.00482	0.000525	0.000303	0.211707	PTPRCAP
M64595	0.00482	0.000525	0.004436	0.170959	RAC2
S59049	0.001377	0.000525	0.000915	-0.61362	RGS1
AL050267	0.00482	0.000525	0.000204	0.311003	SAMHD1
W28498	0.00482	0.000525	1.7E-05	-0.57386	SAR1
W27050	0.00482	0.000525	2.37E-05	-0.587	SFPQ
X92762	0.00482	0.000525	0.000116	0.283179	TAZ
U18422	0.001377	0.000525	0.000279	-0.14486	TFDP2
D87127	0.001377	0.000525	0.000126	-0.32216	TLOC1
U12595	0.001377	0.000525	1.07E-05	0.347309	TRAP1
AF046024	0.00482	0.000525	0.000469	0.405378	UBE1C
AF032456	0.001377	0.000525	5.89E-05	0.269833	UBE2G2
Y09723	0.00482	0.000525	0.000854	-0.23772	ZNF151
AL031778	0.00482	0.000525	0.000239	0.178561	
AL049218	0.00482	0.000525	0.001951	0.238837	
AL080216	0.00482	0.000525	0.000349	0.311531	
L00352	0.00482	0.000525	0.005084	-0.39882	
S79267	0.00482	0.000525	0.000908	-0.19945	
U94902	0.00482	0.000525	0.002556	-0.17833	
AA206524	0.000344	0.000567	0.000172	0.161868	BART1
AA926959	0.000344	0.000567	8.47E-05	0.169915	CKS1
M27543	0.000344	0.000567	0.000319	-0.48924	GNAI3
AF019386	0.000344	0.000567	0.000399	-0.18103	HS3ST1
AB006537	0.000344	0.000567	0.000658	-0.1547	IL1RAP
AJ001306	0.000344	0.000567	5.7E-05	0.338818	INADL
AB011116	0.000344	0.000567	0.000355	0.25593	KIAA0544
AB029014	0.000344	0.000567	0.001352	-0.1261	KIAA1091
AB029027	0.000344	0.000567	0.00209	0.180974	KIAA1104
M10901	0.000344	0.000567	4E-05	-0.42455	NR3C1
D30036	0.000344	0.000567	5.62E-05	-0.15539	PITPN
U47077	0.000344	0.000567	0.001173	0.30799	PRKDC
AF006751	0.000344	0.000567	3.4E-05	-0.23462	RRBP1
AB006198	0.000344	0.000567	0.001465	0.256734	SART1
D63780	0.000344	0.000567	0.00021	0.374406	STK25
W28892	0.000344	0.000567	8.26E-05	0.803602	SUI1
M74524	0.000344	0.000567	0.000421	-0.31531	UBE2A
AL031230	0.000344	0.000567	6.83E-05	0.272378	
AF057160	0.001377	0.000588	0.000279	0.307281	ADPRTL1
M74491	0.001377	0.000588	3.02E-05	0.170825	ARF3
AL120559	0.001377	0.000588	4.8E-05	-0.64478	ARPP-19
D13630	0.001377	0.000588	3.01E-05	-0.42457	BZAP45
U83246	0.001377	0.000588	0.003502	0.133045	CPNE1
AL050390	0.001377	0.000588	0.000139	0.231898	DKFZP564O043
D13315	0.001377	0.000588	0.000203	0.371377	GLO1
H12458	0.001377	0.000588	5.42E-05	-0.22578	H12458 yj12d03.s1

AI347088	0.001377	0.000588	0.000151	0.321012	HMG17L3
X59770	0.001377	0.000588	0.001417	-0.36292	IL1R2
AB007855	0.000344	0.000588	1.02E-05	0.086396	KIAA0395
AB016816	0.001377	0.000588	0.000751	0.146218	MASL1
U07132	0.001377	0.000588	0.002035	-0.27336	NR1H2
AB019409	0.001377	0.000588	0.001479	0.154377	PDL-108
AB020641	0.001377	0.000588	0.00342	0.174568	PFTK1
AL050259	0.001377	0.000588	0.001864	0.272972	RAB2L
AA099265	0.001377	0.000588	0.000614	0.38275	RECK
X75042	0.001377	0.000588	6.85E-05	-0.39572	REL
AL050290	0.001377	0.000588	0.002426	-0.28771	SAT
AJ006417	0.001377	0.000588	0.000125	-0.18595	TBCD
X02812	0.001377	0.000588	1.78E-05	-0.16423	TGFB1
AL050262	0.001377	0.000588	0.0031	0.348226	TLR1
X16576	0.001377	0.000588	9.49E-05	0.431692	ZNF46
X91249	0.000344	0.000609	1.04E-05	-0.3925	ABCG1
Y00486	0.000344	0.000609	0.000297	0.259418	APRT
U10473	0.000344	0.000609	0.000103	-0.15424	B4GALT1
AB014595	0.000344	0.000609	5.19E-05	0.320955	CUL4B
Y15227	0.000344	0.000609	4.08E-05	0.222481	DLEU1
U85267	0.000344	0.000609	0.000131	0.142894	DSCR1
AB019036	0.000344	0.000609	0.000336	0.177649	GGPS1
U90313	0.000344	0.000609	0.001838	-0.25377	GSTTLp28
L42243	0.000344	0.000609	0.000201	0.403838	HUMIFNAM08
X16983	0.000344	0.000609	0.000317	0.232935	ITGA4
AB002368	0.000344	0.000609	0.001709	0.215217	KIAA0370
AI521453	0.000344	0.000609	0.000707	-0.22735	PC4
Y08110	0.000344	0.000609	9.87E-05	0.260436	SORL1
D38122	0.000344	0.000609	6.27E-05	-0.61781	TNFSF6
U49278	0.000344	0.000609	0.000173	0.204424	UBE2V1
X99050	0.000344	0.000609	7.72E-05	0.289751	UVRAG
Z93930	0.000344	0.000609	0.00015	-0.26558	XBP1
AF015767	0.000344	0.000659	0.000199	0.578977	BRE
M34677	0.000344	0.000659	0.000647	0.198622	F8A
J00210	0.000344	0.000659	0.002453	-0.18828	IFNA1
AJ007583	0.000344	0.000659	0.00506	-0.12644	LARGE
M36881	0.000344	0.000659	0.000302	0.328248	LCK
X70326	0.000344	0.000659	0.000132	-0.58974	MACMARCKS
M64571	0.000344	0.000659	0.000158	0.157573	MAP4
AI345944	0.000344	0.000659	0.000363	0.311507	NDUFB1
D23662	0.000344	0.000659	0.000171	0.289452	NEDD8
M14630	0.000344	0.000659	1.26E-05	-0.1626	PTMA
D64015	0.000344	0.000659	0.001012	0.195679	TIAL1
M63582	0.000344	0.000659	2.66E-05	-0.39175	
U79300	0.000344	0.000659	0.000196	-0.16218	
D29805	0.00482	0.000812	0.000289	-0.23044	B4GALT1
U47414	0.001377	0.000812	0.000137	0.262974	CCNG2
L33930	0.001377	0.000812	5.56E-06	0.343203	CD24
AL050164	0.00482	0.000812	0.000345	0.307729	CDYL
D10040	0.001377	0.000812	1.49E-05	-0.45708	FACL2

M36820	0.00482	0.000812	7.67E-05	-0.49075	GRO2
U77948	0.00482	0.000812	0.000511	0.286776	GTF2I
X56681	0.00482	0.000812	0.000503	-0.18359	JUND
AF070569	0.00482	0.000812	0.000446	-0.6104	MGC14376
W28205	0.00482	0.000812	0.00017	-0.21741	MKLN1
U61981	0.001377	0.000812	0.000725	0.203996	MSH3
AB014547	0.001377	0.000812	7.73E-05	0.217806	MTMR4
AL050366	0.00482	0.000812	0.001126	0.421541	OGT
U89606	0.001377	0.000812	6.13E-05	-0.19512	PDXK
D10495	0.00482	0.000812	0.000433	0.290156	PRKCD
D42063	0.001377	0.000812	0.000346	-0.52828	RANBP2
H68340	0.00482	0.000812	0.004081	-0.3419	RNAHP
AF059617	0.001377	0.000812	0.00012	-0.27807	SNK
AB028950	0.00482	0.000812	0.000365	0.313606	TLN1
L41690	0.001377	0.000812	0.000109	0.401776	TRADD
X95384	0.00482	0.000812	0.00053	0.327055	UK114
X98054	0.00482	0.001094	4.71E-05	-0.12615	CREBL1
J05036	0.00482	0.001094	0.00171	0.064463	CTSE
AF001434	0.00482	0.001094	0.000161	-0.26223	EHD1
L18960	0.00482	0.001094	3.26E-05	-0.38369	EIF1A
AB014555	0.00482	0.001094	0.001608	-0.18202	KIAA0655
X76057	0.00482	0.001094	0.000352	0.193745	MPI
X74594	0.00482	0.001094	0.000352	0.439326	RBL2
AF044309	0.00482	0.001094	0.000217	-0.2163	STX11
U07158	0.00482	0.001094	0.000122	-0.2301	STX4A
L40386	0.00482	0.001094	7.97E-05	-0.19863	TFDP2
H97470	0.00482	0.001094	0.000624	-0.10587	
U78027	0.00482	0.001094	0.000804	0.340784	
U50534	0.001377	0.001345	0.00039	0.250627	13CDNA73
X55330	0.001377	0.001345	9.3E-05	0.493025	AGA
L19605	0.001377	0.001345	0.004442	0.183134	ANXA11
Y00097	0.001377	0.001345	4.42E-05	0.409932	ANXA6
U26455	0.00482	0.001345	0.000705	0.499049	ATM
AF047473	0.001377	0.001345	5.14E-05	0.226	BUB3
M95724	0.00482	0.001345	0.002166	-0.46553	CENPC1
AB014558	0.001377	0.001345	0.004662	-0.44793	CRY2
R38263	0.001377	0.001345	0.00048	-0.12843	DJ347H13.4
AI434146	0.001377	0.001345	0.000397	0.187485	DKFZp570I0164
D12686	0.00482	0.001345	0.008744	-0.11456	EIF4G1
AF059611	0.00482	0.001345	0.000694	-0.27343	ENC1
X59834	0.001377	0.001345	0.004986	-0.34836	GLUL
D64142	0.001377	0.001345	0.000169	0.293999	H1FX
U51333	0.001377	0.001345	0.000376	0.273402	HK3
M59488	0.001377	0.001345	0.001357	-0.13313	HUMS100B3
X58529	0.001377	0.001345	0.000417	1.04789	IGHM
D79983	0.001377	0.001345	2.97E-05	0.387491	KIAA0161
AB002370	0.00482	0.001345	0.00052	0.425557	KIAA0372
AB007863	0.001377	0.001345	0.000128	0.29668	KIAA0403
AB014549	0.001377	0.001345	0.001505	0.42387	KIAA0649
AB020711	0.00482	0.001345	0.002079	0.222346	KIAA0904

AB002357	0.001377	0.001345	0.001045	0.317849	KIF3B
U09284	0.00482	0.001345	0.000792	-0.23635	LIMS1
D50810	0.001377	0.001345	5.17E-05	-0.1859	LNPEP
U18259	0.001377	0.001345	0.000153	0.229322	MHC2TA
AF041080	0.00482	0.001345	0.001964	0.367098	MN7
X70991	0.001377	0.001345	0.00203	-0.14032	NAB2
AC002045	0.00482	0.001345	0.00028	0.326033	NPIP
U92538	0.001377	0.001345	0.00149	0.2372	ORC5L
U24153	0.001377	0.001345	0.00018	-0.36291	PAK2
Z49194	0.001377	0.001345	0.000519	0.215733	POU2AF1
AF016371	0.001377	0.001345	0.001059	0.240562	PPIH
AF020736	0.001377	0.001345	6.26E-05	-0.32893	PSMC4
D11327	0.001377	0.001345	0.00019	-0.74969	PTPN7
AF098799	0.00482	0.001345	0.001893	-0.3646	RANBP7
M22995	0.001377	0.001345	0.005586	0.270032	RAP1A
L11566	0.001377	0.001345	0.000291	0.17032	RPL18
U71364	0.001377	0.001345	0.000276	-0.24064	SERPINB9
X07834	0.00482	0.001345	0.000362	-0.21917	SOD2
X05839	0.001377	0.001345	0.000779	-0.20819	TGFB1
AB000509	0.001377	0.001345	3.63E-05	0.460686	TRAF5
U82130	0.001377	0.001345	4.69E-05	-0.36064	TSG101
L16842	0.001377	0.001345	0.001533	0.189597	UQCRC1
X51521	0.001377	0.001345	0.000379	-0.62845	VIL2
M86400	0.001377	0.001345	0.000132	-0.30595	YWHAZ
AF041259	0.001377	0.001345	0.001393	0.202001	ZNF217
AA977136	0.001377	0.001345	0.001953	0.095364	
AI624038	0.001377	0.001345	0.001833	-0.16137	
AL050148	0.00482	0.001345	0.000905	0.266795	
HG2709-HT2805	0.001377	0.001345	0.000134	-0.22645	
HG3227-HT3404	0.001377	0.001345	4.02E-05	-0.23244	
M28225	0.00482	0.001345	0.001444	-0.95152	
U80017	0.001377	0.001345	0.004917	0.171432	
X55544	0.001377	0.001467	0.001049	-0.12406	ATF1
X52560	0.001377	0.001467	8.17E-05	-0.50375	CEBPB
AA044787	0.001377	0.001467	0.001147	0.289086	CNOT8
AF017790	0.001377	0.001467	6.88E-06	0.382661	HEC
D00749	0.001377	0.001467	0.000131	-0.10539	HUMCD7G3
AB007890	0.001377	0.001467	0.000838	0.200677	KIAA0430
L35251	0.001377	0.001467	0.000873	0.12909	MFAP3
AF098638	0.001377	0.001467	0.000684	-0.18761	RAB5EP
AB004857	0.001377	0.001467	0.000471	0.23048	SLC11A2
U53347	0.001377	0.001467	0.001367	-0.13658	SLC1A5
U04847	0.001377	0.001467	0.000403	0.117176	SMARCB1
M92843	0.001377	0.001467	3.3E-05	-1.37866	ZFP36
AF033199	0.001377	0.001467	0.00019	0.237743	ZNF204
AC004893	0.001377	0.001467	0.000617	-0.25759	
AL050151	0.001377	0.001467	8.03E-06	-0.80887	
U80770	0.001377	0.001467	0.006738	-0.12644	
W27675	0.00482	0.001614	0.005157	0.468709	CDA02
AI056696	0.00482	0.001614	0.000665	0.215941	CETN3

AF062536	0.00482	0.001614	0.005001	0.197482	CUL1
D29643	0.00482	0.001614	0.0005	0.157183	DDOST
AA181196	0.00482	0.001614	0.000166	0.119162	FLJ11712
W07033	0.001377	0.001614	0.000136	0.347648	GMFG
Z18859	0.00482	0.001614	0.000684	0.181514	GNAT2
U83660	0.00482	0.001614	0.00114	0.136411	HSU83660
AA628946	0.00482	0.001614	0.002684	0.337197	KHSRP
D13626	0.00482	0.001614	0.005837	0.254138	KIAA0001
AB002340	0.00482	0.001614	0.002977	0.168464	KIAA0342
AB002353	0.001377	0.001614	0.000119	0.305921	KIAA0355
U32849	0.00482	0.001614	0.000272	0.345048	NMI
S79219	0.00482	0.001614	0.000119	0.167463	PCCA
L37127	0.00482	0.001614	0.010173	0.103446	POLR2J
M35416	0.00482	0.001614	0.001433	0.33505	RALB
X76061	0.00482	0.001614	0.000273	0.378113	RBL2
AF061741	0.00482	0.001614	0.004586	0.221278	SDR1
D31891	0.001377	0.001614	0.000819	0.161458	SETDB1
W26406	0.00482	0.001614	0.000479	0.300512	SIAH1
X84002	0.00482	0.001614	0.000699	0.143479	TAF2J
U81006	0.00482	0.001614	0.003151	0.255479	TM9SF2
U69108	0.00482	0.001614	0.000657	0.208286	TRAF5
S66666	0.00482	0.001614	0.002417	0.119478	
U84388	0.00482	0.001719	0.000197	-0.18606	CRADD
L08069	0.00482	0.001719	0.001985	-0.31866	DNAJA1
U41514	0.00482	0.001719	9.38E-05	-0.44803	GALNT1
M69013	0.001377	0.001719	6.26E-05	-0.1948	GNA11
L11706	0.00482	0.001719	0.001422	-0.16675	LIPE
R92331	0.00482	0.001719	0.000198	-0.24196	MT1E
X64318	0.00482	0.001719	0.006253	-0.37391	NFIL3
X12458	0.00482	0.001719	0.001489	-0.33668	P3
M25393	0.00482	0.001719	0.000958	-0.23304	PTPN2
M59465	0.00482	0.001719	0.0002	-0.96074	TNFAIP3
AF084260	0.00482	0.001719	0.001063	-0.39491	TRIP15
HG2149-HT2219	0.00482	0.001719	0.001437	-0.14432	
AB021663	0.00482	0.001963	0.00027	-0.13923	ATF5
AL080209	0.00482	0.001963	0.000337	0.437957	DKFZP586F2423
M34641	0.00482	0.001963	0.002352	-0.14552	FGFR1
AL096714	0.001377	0.001963	0.000469	0.224782	FLJ20113
AB011124	0.001377	0.001963	0.000101	-0.17709	KIAA0552
AB020633	0.001377	0.001963	0.00082	0.308616	KIAA0826
AB029020	0.001377	0.001963	0.00061	0.3824	KIAA1097
X76220	0.001377	0.001963	7.21E-05	0.444366	MAL
AF040964	0.00482	0.001963	0.001161	-0.54746	MGC4701
U91512	0.001377	0.001963	0.00035	-0.55826	NINJ1
U60325	0.00482	0.001963	0.000288	-0.14386	POLG
Z15108	0.001377	0.001963	0.000107	0.176424	PRKCZ
Y08262	0.001377	0.001963	0.000183	0.377974	SCA2
U30246	0.001377	0.001963	0.000209	-0.25952	SLC12A2
J04137	0.001377	0.001963	0.000641	-0.22175	SSA2
M38449	0.001377	0.001963	0.0004	-0.29059	TGFB1

AC005757	0.00482	0.001963	0.000169	0.387439	
HG825-HT825	0.001377	0.001963	0.000553	-0.19964	
AF047348	0.001377	0.002207	0.000292	0.202669	APBA2
AF053977	0.001377	0.002207	0.003143	0.134266	CDC23
AF083322	0.001377	0.002207	0.000344	0.272282	CEP1
AL050369	0.001377	0.002207	0.001224	0.241992	DKFZP566J153
D32257	0.001377	0.002207	0.000238	0.300058	GTF3A
M65217	0.001377	0.002207	0.000232	0.249614	HSF2
AB014574	0.001377	0.002207	0.000606	0.130056	KIAA0674
AB029023	0.001377	0.002207	0.000219	0.219428	KIAA1100
Z34975	0.001377	0.002207	8.88E-05	0.41432	LDLC
D83597	0.001377	0.002207	0.000136	0.249838	LY64
U09759	0.001377	0.002207	0.000842	0.330751	MAPK9
U59302	0.001377	0.002207	0.000241	0.309348	NCOA1
AJ005698	0.001377	0.002207	0.004173	0.139618	PARN
X54871	0.001377	0.002207	0.010035	0.119258	RAB5B
AL080198	0.001377	0.002207	0.002866	0.251598	RENT2
M74447	0.001377	0.002207	0.000444	0.093537	TAP2
J04973	0.001377	0.002207	0.011696	0.141705	UQCRC2
U90902	0.001377	0.002207	0.001336	0.246217	
U94333	0.001377	0.002323	0.004818	-0.13898	C1QR
U60808	0.001377	0.002323	0.000374	-0.12217	CDS1
L08069	0.001377	0.002323	0.002161	-0.29982	DNAJA1
AA552140	0.001377	0.002323	0.003368	-0.22604	E2F4
M31210	0.001377	0.002323	0.000124	-0.33555	EDG1
AI189287	0.001377	0.002323	0.002445	-0.24115	H1F2
W25934	0.001377	0.002323	0.003385	-0.32382	JTV1
Z98046	0.001377	0.002323	0.000122	-0.33551	MAGED2
L76571	0.001377	0.002323	0.009985	-0.12617	NR0B2
AF071504	0.001377	0.002323	0.000191	-0.14267	STX11
X56687	0.001377	0.002323	0.00011	-0.29728	UBTF
AI097085	0.001377	0.002323	0.000941	-0.16209	
AA114830	0.001377	0.002503	0.000293	0.272601	AKAP10
AI991631	0.001377	0.002503	0.000132	-0.11786	BRD4
U04343	0.001377	0.002503	4.45E-05	-0.25478	CD86
M12824	0.001377	0.002503	0.008271	-0.34597	CD8A
U89896	0.001377	0.002503	0.006997	-0.2182	CSNK1G2
AI432401	0.001377	0.002503	0.006072	0.32631	FGL2
AA176780	0.001377	0.002503	0.001296	0.14235	HSA249128
M21188	0.001377	0.002503	0.000165	0.251899	IDE
U43572	0.001377	0.002503	0.000128	0.318327	NAGLU
X02751	0.001377	0.002503	0.000359	-0.2229	NRAS
AF069250	0.001377	0.002503	0.00135	0.476217	OA48-18
D25328	0.001377	0.002503	0.000171	0.125335	PFKP
AF010312	0.001377	0.002503	0.001216	-0.47628	PIG7
M34668	0.001377	0.002503	0.000421	0.181315	PTPRA
AF061836	0.001377	0.002503	0.001026	0.21847	RASSF1
AI535653	0.001377	0.002503	0.001712	0.34571	SC4MOL
X75755	0.001377	0.002503	0.003813	-0.2236	SFRS2
W16505	0.001377	0.002503	0.001699	0.101763	SNRPD2

L31529	0.001377	0.002503	0.000325	0.144265	SNTB1
D86970	0.001377	0.002503	0.000219	0.218777	TIAF1
AL050223	0.001377	0.002503	0.002632	0:2458	VAMP2
AA877215	0.001377	0.002503	0.008439	-0.17878	
AL049435	0.001377	0.002503	0.000111	0.194323	
M76180	0.001377	0.002575	0.000698	0.162775	DDC
M94065	0.001377	0.002575	0.000426	0.156894	DHODH
J04988	0.001377	0.002575	6.17E-05	-0.22304	HSPCB
Z68907	0.001377	0.002575	0.000305	0.391111	IDH3G
J03909	0.001377	0.002575	0.000837	-0.35709	IFI30
AB011104	0.001377	0.002575	0.000729	0.227798	KIAA0532
AB011173	0.001377	0.002575	0.000585	0.283714	KIAA0601
U70322	0.001377	0.002575	0.000177	-0.41259	KPNB2
D86961	0.001377	0.002575	0.001925	-0.19403	LHFPL2
AF052111	0.001377	0.002575	0.000738	0.249468	LOC51172
AJ224875	0.001377	0.002575	0.005091	0.139606	MGC2840
M21985	0.001377	0.002575	0.001409	-0.102	NR2C1
J05448	0.001377	0.002575	0.004982	-0.15329	POLR2C
AB006572	0.001377	0.002575	0.000169	0.213636	RMP
AJ011712	0.001377	0.002575	0.011372	0.066711	TNNT1
AJ006973	0.001377	0.002575	0.000101	-0.31773	TOM1
U67122	0.001377	0.002575	0.000364	-0.14274	UBL1
U71598	0.001377	0.002575	0.003508	0.128607	ZNF274
M81118	0.001377	0.002575	0.00023	0.333526	
U61166	0.001377	0.002575	0.003055	-0.14488	
U94902	0.001377	0.002575	0.000137	-0.23298	
Z82244	0.001377	0.002575	0.000258	-0.53938	
M36341	0.001377	0.002788	0.00056	-0.38498	ARF4
L09159	0.001377	0.002788	0.00112	0.474985	ARHA
U68485	0.00482	0.002788	0.006797	0.224774	BIN1
Z22555	0.001377	0.002788	0.005455	-0.16351	CD36L1
D44497	0.00482	0.002788	0.004453	0.131654	CORO1A
L37042	0.00482	0.002788	0.000582	-0.33273	CSNK1A1
M74099	0.001377	0.002788	0.00014	0.389638	CUTL1
AL080159	0.001377	0.002788	0.002335	-0.11101	DKFZP434M154
AF004292	0.001377	0.002788	0.001306	-0.2375	DKFZP566C134
AF088982	0.001377	0.002788	0.001264	-0.22098	DNAJB5
U73704	0.001377	0.002788	0.001412	-0.17508	FAP48
M77810	0.00482	0.002788	0.000209	-0.15854	GATA2
U67369	0.00482	0.002788	0.00347	0.137095	GFI1
D00632	0.001377	0.002788	0.001138	-0.15517	GPX3
X99270	0.001377	0.002788	0.00065	0.191612	HSXQ28ORF
D42041	0.00482	0.002788	0.003705	0.195279	KIAA0088
AA524058	0.001377	0.002788	0.000288	0.360599	LOC51020
U77604	0.001377	0.002788	0.00233	0.296247	MGST2
J04031	0.00482	0.002788	0.000148	0.290038	MTHFD1
AF025794	0.001377	0.002788	0.006763	0.107466	MTRR
D86326	0.001377	0.002788	0.008217	0.124987	P115
U14417	0.001377	0.002788	0.000521	-0.13999	RALGDS
U85611	0.001377	0.002788	0.000126	-0.3879	SIP2-28

U66617	0.001377	0.002788	0.001462	-0.14653	SMARCD1
X59960	0.001377	0.002788	0.005127	-0.11069	SMPD1
AF031166	0.001377	0.002788	0.001219	0.110457	SRP46
U86136	0.001377	0.002788	0.000542	0.149235	TEP1
U16296	0.001377	0.002788	0.00138	0.136848	TIAM1
D50917	0.001377	0.002788	0.000467	0.402091	TRIP-Br2
AC004770	0.001377	0.002788	0.001042	-0.10615	
J03071	0.001377	0.002788	0.0116	0.17732	
D67031	0.00482	0.004163	0.000204	0.543743	ADD3
U68030	0.00482	0.004163	0.000279	-0.16075	CCR6
U41387	0.00482	0.004163	8.67E-05	-0.29576	DDX21
AF084535	0.00482	0.004163	0.002306	0.159095	EPM2A
AI417075	0.00482	0.004163	0.000538	0.330385	FLJ14040
D82348	0.00482	0.004349	0.006063	0.245422	ATIC
AA648295	0.00482	0.004349	0.002422	0.337484	CBX3
U79270	0.00482	0.004349	0.001345	0.460807	COX11
AF071748	0.00482	0.004349	0.002471	0.170315	CTSF
AL080088	0.00482	0.004349	0.000207	0.165357	DKFZP564K2062
AI540318	0.00482	0.004349	0.00055	-0.13789	DNAJB6
U03272	0.00482	0.004349	0.003893	0.101031	FBN2
Z97989	0.00482	0.004349	0.001126	-0.41969	FYN
AF042379	0.00482	0.004349	0.008308	0.176604	GCP2
U73737	0.00482	0.004349	0.00262	-0.14396	HUMMSH06
AF031167	0.00482	0.004349	0.000117	0.201914	IL15
D83778	0.00482	0.004349	0.000504	-0.2149	KIAA0194
AB028965	0.00482	0.004349	0.007277	0.125446	KIAA1042
M79321	0.00482	0.004349	0.003247	-0.21992	LYN
L11284	0.00482	0.004349	0.003994	-0.09508	MAP2K1
AJ000882	0.00482	0.004349	0.00042	0.180413	NCOA1
L41067	0.00482	0.004349	0.000388	0.370635	NFATC3
AF057297	0.00482	0.004349	0.001191	0.521103	OAZ2
X66360	0.00482	0.004349	0.001123	-0.17473	PCTK2
U24183	0.00482	0.004349	0.001156	0.141168	PFKM
L42373	0.00482	0.004349	0.006706	0.165885	PPP2R5A
AB018288	0.00482	0.004349	0.003777	0.184227	RANBP16
M58459	0.00482	0.004349	0.008923	-1.04752	RPS4Y
M60725	0.00482	0.004349	0.001349	-0.10092	RPS6KB1
Y10931	0.00482	0.004349	0.001246	0.194156	SPK
AB004904	0.00482	0.004349	0.000233	-0.31373	SSI-3
AF060798	0.00482	0.004349	0.000809	0.142845	STK16
U66867	0.00482	0.004349	0.011318	0.150812	UBE2I
AB028980	0.00482	0.004349	0.001471	0.265042	USP24
AF052107	0.00482	0.004349	0.002884	0.197902	
AL031985	0.00482	0.004349	0.000181	-0.24089	
D26121	0.00482	0.004349	0.00387	-0.16268	
W28667	0.00482	0.004349	0.004391	0.476395	
AL050157	0.00482	0.004467	0.000289	0.269949	DKFZP586O0120
U31930	0.00482	0.004467	0.000244	0.349997	DUT
AI951946	0.00482	0.004467	8.71E-05	0.401112	HBOA
AB002354	0.00482	0.004467	0.001517	-0.13368	KIAA0356

M36067	0.00482	0.004467	8.15E-05	0.277858	LIG1
J02783	0.00482	0.004467	0.002151	-0.21979	P4HB
M37238	0.00482	0.004467	0.005333	-0.15474	PLCG2
M99438	0.00482	0.004467	6.2E-05	-0.36844	TLE3
Z97630	0.00482	0.004467	0.002794	0.217849	
D14874	0.00482	0.005608	0.000611	-0.55358	ADM
L08177	0.00482	0.005608	0.000434	-0.49252	EBI2
U09510	0.00482	0.005608	5.27E-05	-0.57567	GARS
L05424	0.00482	0.005608	0.000114	-0.39048	HUMSCG19
X13956	0.00482	0.005608	0.004098	0.187622	MGC10471
U88620	0.00482	0.005608	0.00074	0.345628	OGG1
M29551	0.00482	0.005608	0.000471	0.319301	PPP3CB
AF068836	0.00482	0.005608	0.000323	-0.23628	PSCDBP
U08316	0.00482	0.005608	0.0006	0.205899	RPS6KA3
J02966	0.00482	0.005608	0.000498	-0.11291	SLC25A4
AF107463	0.00482	0.005608	0.002824	-0.36924	SPF30
AB000450	0.00482	0.005608	0.000256	-0.24717	VRK2
AF070590	0.00482	0.005608	0.000834	0.127523	
AF001383	0.00482	0.006065	0.002075	0.16512	BIN1
AF026291	0.00482	0.006065	0.000385	-0.16859	CCT4
D63877	0.00482	0.006065	0.005226	-0.13956	KIAA0157
U14383	0.00482	0.006065	0.002623	-0.18669	MUC8
U68140	0.00482	0.006065	0.000677	0.172443	NVL
L25441	0.00482	0.006065	0.000613	-0.17207	PGGT1B
U46751	0.00482	0.006065	0.000578	-0.38675	SQSTM1
HG4740-HT5187	0.00482	0.006065	0.00867	0.146562	
W26851	0.00482	0.006065	0.002052	0.312992	
U78735	0.00482	0.006347	0.000529	-0.09197	ABCA3
Y12226	0.00482	0.006347	0.000397	-0.21303	AP1G1
D38293	0.00482	0.006347	0.002894	-0.24373	AP3M2
X14046	0.00482	0.006347	0.001084	0.134786	CD37
AF026004	0.00482	0.006347	0.008622	-0.07494	CLCN2
U46023	0.00482	0.006347	0.000273	-0.17969	CXorf6
AL080178	0.00482	0.006347	0.000683	0.260343	DKFZP434K171
AL080118	0.00482	0.006347	0.001904	-0.28696	DKFZP564F1123
AL050197	0.00482	0.006347	0.004294	0.233045	DKFZP586D0623
X68277	0.00482	0.006347	0.011411	-0.42385	DUSP1
X03674	0.00482	0.006347	0.008478	0.174463	G6PD
Y13286	0.00482	0.006347	0.004068	0.134985	GDI2
U19247	0.00482	0.006347	0.000589	-0.29688	HSINFGRA7
AB023163	0.00482	0.006347	0.002537	0.194491	HYPH
L36818	0.00482	0.006347	0.007182	0.204818	INPPL1
U51127	0.00482	0.006347	0.003952	0.108702	IRF5
M15395	0.00482	0.006347	0.001863	0.402323	ITGB2
U51336	0.00482	0.006347	0.008615	0.336527	ITPK1
AJ000008	0.00482	0.006347	0.000256	-0.14181	PIK3C2G
AI126004	0.00482	0.006347	0.000954	0.262925	SAS10
AF051325	0.00482	0.006347	0.000144	-0.43952	SH2D2A
U79528	0.00482	0.006347	0.002518	0.158101	SR-BP1
U52426	0.00482	0.006347	9.31E-05	0.411984	STIM1

AB018339	0.00482	0.006347	0.000751	0.199758	SYNE-1B
D43642	0.00482	0.006347	0.0005	0.305805	TCFL1
D29767	0.00482	0.006347	0.003934	-0.09702	TEC
M92383	0.00482	0.006347	0.001466	0.219769	TMSB10
AA192359	0.00482	0.006347	0.00028	0.17619	TRN-SR
AC004472	0.00482	0.006347	0.002169	-0.15115	
AF052138	0.00482	0.006347	0.000189	0.441167	
X15674	0.00482	0.006347	0.007899	-0.10738	
Z82215	0.00482	0.006347	0.002527	0.153792	
AF070523	0.00482	0.006634	0.00037	0.437983	JWA
D13641	0.00482	0.006634	0.000776	0.275308	KIAA0016
X79204	0.00482	0.006634	0.000182	0.256049	SCA1
AB015718	0.00482	0.006634	0.001172	0.202412	STK10
AF059575	0.00482	0.006634	0.000563	-0.18074	
M74089	0.00482	0.006634	0.00076	0.187888	
U44111	0.00482	0.006634	0.003845	0.105361	
AJ243310	0.00482	0.006921	0.000945	-0.97643	C14orf3
W26854	0.00482	0.006921	0.011098	-0.13774	DKFZP434D156
U88629	0.00482	0.006921	0.001778	-0.16763	ELL2
M59830	0.00482	0.006921	0.000221	-1.12882	HSPA1B
M95929	0.00482	0.006921	0.004606	-0.34536	PMX1
M57399	0.00482	0.006921	0.010231	-0.14331	PTN
N25117	0.00482	0.006921	0.002068	-0.16335	RPS26
AL049940	0.00482	0.006921	0.001149	-0.42489	RYBP
U39318	0.00482	0.006921	0.001097	-0.24533	UBE2D3
Z29331	0.00482	0.006921	0.000193	-0.15851	UBE2H
M55682	0.00482	0.006921	0.010264	-0.10921	
S58544	0.00482	0.006921	0.005501	-0.11193	
L13687	0.00482	0.007311	0.002185	0.114008	ARL2
M88714	0.00482	0.007311	0.002075	0.114833	BDKRB2
AL050173	0.00482	0.007311	0.001866	0.128954	C21orf25
M33680	0.00482	0.007311	0.002612	0.134487	CD81
X05299	0.00482	0.007311	0.003837	0.171613	CENPB
X16832	0.00482	0.007311	0.000578	0.177395	CTSH
U83410	0.00482	0.007311	0.005207	0.219569	CUL2
AL050018	0.00482	0.007311	0.003938	0.220539	DKFZP564B116
AL080063	0.00482	0.007311	0.006562	0.186332	DKFZP564I052
AL050286	0.00482	0.007311	0.000767	0.221397	DKFZP586A011
X63692	0.00482	0.007311	0.003174	0.172997	DNMT1
AA522537	0.00482	0.007311	0.002762	0.113812	ELAC2
AI183417	0.00482	0.007311	0.006167	0.101739	GABPB1
X62534	0.00482	0.007311	0.000973	0.195089	HMG2
D50532	0.00482	0.007311	0.001268	0.159735	HML2
AJ006591	0.00482	0.007311	0.001379	0.1682	HSA6591
Y00796	0.00482	0.007311	0.000438	0.386166	ITGAL
AB018301	0.00482	0.007311	0.008701	0.138344	KIAA0758
AB020694	0.00482	0.007311	0.002526	0.205561	KIAA0887
AB023198	0.00482	0.007311	0.000409	0.275051	KIAA0981
AB028958	0.00482	0.007311	0.001533	0.117614	KIAA1035
U66711	0.00482	0.007311	0.006567	0.260368	LY6E

L13744	0.00482	0.007311	0.007658	0.19599	MLLT3
Y09631	0.00482	0.007311	0.000769	0.309898	PIBF1
L77213	0.00482	0.007311	0.001122	0.247214	PMVK
X73478	0.00482	0.007311	0.000681	0.242238	PPP2R4
U94319	0.00482	0.007311	0.000688	0.337656	PSIP2
U27516	0.00482	0.007311	0.000222	0.194938	RAD52
W25793	0.00482	0.007311	0.000438	0.258505	RNF3
X06617	0.00482	0.007311	0.002581	0.116631	RPS11
Z25749	0.00482	0.007311	0.001419	0.123333	RPS7
U80760	0.00482	0.007311	0.007371	0.161214	TNRC1
L27071	0.00482	0.007311	0.000638	0.372837	TXK
AL031427	0.00482	0.007311	0.000541	0.367004	
AL109722	0.00482	0.007311	0.00187	0.134304	
X15675	0.00482	0.007311	0.011165	0.131908	
AL050089	0.00482	0.007852	0.001906	-0.23061	BAZ1A
L22005	0.00482	0.007852	0.002439	-0.22532	CDC34
AB014679	0.00482	0.007852	0.003059	-0.13664	CHST2
X77956	0.00482	0.007852	0.000689	-0.22743	ID1
AI814466	0.00482	0.007852	0.001127	-0.1955	VAMP5
HG4074-HT4344	0.00482	0.007852	0.000964	-0.17461	
AF005050	0.00482	0.008059	0.001761	0.230395	DNPEP
J03909	0.00482	0.008059	0.000125	-0.18353	IFI30
X59841	0.00482	0.008059	0.000226	0.265756	PBX3
AI819942	0.00482	0.009314	0.002286	0.326115	2-Sep
D86981	0.00482	0.009314	0.003441	0.319525	APPBP2
Y10805	0.00482	0.009314	0.002583	0.183496	HRMT1L2
U51127	0.00482	0.009314	0.00212	0.282678	IRF5
U14970	0.00482	0.009314	0.000561	0.144991	RPS5
AI813532	0.00482	0.009314	0.00037	-0.41933	TNFRSF1B
Y15228	0.00482	0.010363	0.002026	-0.17032	DLEU2
AA926957	0.00482	0.010363	0.000909	-0.22483	FLJ10534
AA554945	0.00482	0.010363	0.001827	-0.14301	FLJ10803
AJ001383	0.00482	0.010363	0.001968	-0.3226	LY94
M97676	0.00482	0.010363	0.010011	-0.16313	MSX1
AF002020	0.00482	0.010363	0.001278	-0.1736	NPC1
U25975	0.00482	0.010363	0.000764	-0.24651	PAK2
X66363	0.00482	0.010363	0.000837	-0.4179	PCTK1
D87957	0.00482	0.010363	0.004418	-0.14751	RQCD1
AI610467	0.00482	0.010363	0.000699	-0.17683	SMG1
AJ012008	0.00482	0.010363	0.002571	-0.32997	
AJ012008	0.00482	0.010363	0.001638	-0.16204	

Table II: Gene Expression Profile from PBMCs of MS vs. Healthy- Highest Scoring Genes (Bonfferoni analysis)

Identifier	TNOM PValue	Info PValue	t-Test PValue	Log FoldChange	Symbol
AA203527	1.37131E-05	1.613E-06	1.18E-07	0.281992	RPP20
AA780049	7.44428E-05	2.35E-05	7.39E-07	0.54912	FLJ21439
AA845349	7.44428E-05	0.0001187	7.78E-07	0.457176	TRIP7
AA902713	2.10971E-06	1.993E-06	1.44E-06	0.474378	

AB002344	7.44428E-05	5.915E-05	8.48E-07	-1.00068	KIAA0346
AB002347	2.10971E-06	1.329E-07	7.19E-10	0.371731	KIAA0349
AB002348	1.37131E-05	3.861E-06	2.49E-07	0.576346	KIAA0350
AB002386	2.10971E-06	7.732E-07	5.34E-09	0.586117	EZH1
AB002448	1.37131E-05	5.009E-06	2.45E-07	0.468926	
AB007891	1.37131E-05	3.861E-06	3.99E-05	0.196376	KIAA0431
AB007895	1.37131E-05	5.009E-06	9.61E-07	0.186643	KIAA0435
AB007927	2.10971E-06	1.993E-06	2.12E-07	0.323787	RERE
AB007960	2.10971E-06	9.536E-07	7.96E-06	0.447772	SH3GLB1
AB008775	0.000344298	0.0003041	1.88E-06	-0.80745	AQP9
AB011004	0.000344298	7.048E-06	1.41E-06	-1.34073	UAP1
AB011108	1.37131E-05	5.045E-07	4.39E-07	0.453498	PRP4
AB011113	1.37131E-05	7.048E-06	3.74E-07	0.444795	WDR7
AB011115	1.37131E-05	5.045E-07	3.39E-07	0.382809	KIAA0543
AB011161	2.57282E-08	4.013E-09	9.64E-11	0.63432	PIP5K1C
AB014535	1.37131E-05	5.045E-07	1.04E-06	0.285282	KIAA0635
AB014538	0.000344298	4.67E-05	1.98E-06	-0.63923	KIAA0638
AB014579	1.37131E-05	5.009E-06	6.08E-08	0.367966	MGEA5
AB014608	7.44428E-05	9.644E-05	4.59E-06	0.41494	KIAA0708
AB015019	7.44428E-05	7.048E-06	2.75E-07	-0.24515	BAIAP2
AB018343	1.83773E-09	4.157E-10	9.05E-12	0.383078	KIAA0800
AB023153	2.10971E-06	1.329E-07	1.82E-08	0.895842	KIAA0936
AB023235	7.44428E-05	1.613E-06	1.43E-05	0.311216	KIAA1018
AB026118	0.00137719	0.0001897	4.47E-06	-0.24886	MALT1
AB026436	7.44428E-05	1.613E-06	0.000219	-0.7589	DUSP10
AB028951	2.63714E-07	1.715E-07	8.78E-09	0.543028	KIAA1028
AB028981	2.10971E-06	7.732E-07	5.34E-07	0.282288	KIAA1058
AB029015	2.63714E-07	2.488E-07	5.37E-09	0.695063	PLCE2
AB029038	7.44428E-05	1.613E-06	7.62E-05	0.364386	KIAA1115
AC002400	1.37131E-05	3.06E-05	2.28E-06	-0.25834	UBPH
AF000545	7.44428E-05	5.226E-05	3.48E-06	-0.85393	P2Y10
AF001294	1.37131E-05	7.048E-06	1.23E-06	-0.76359	TSSC3
AF004230	2.63714E-07	1.715E-07	3.06E-07	0.349166	LILRB1
AF005043	7.44428E-05	5.226E-05	2.7E-06	0.408592	PARG
AF007130	2.10971E-06	5.045E-07	2.51E-06	0.391811	LOC54104
AF007142	0.000344298	0.0004443	3.15E-06	0.678734	
AF007151	1.37131E-05	5.045E-07	3.25E-06	0.468343	MMS19L
AF010193	7.44428E-05	2.35E-05	1.26E-07	-1.4705	MADH7
AF010309	1.37131E-05	5.009E-06	7.36E-07	-0.28533	PIG3
AF012023	7.44428E-05	5.915E-05	1.02E-06	0.50623	ICAP-1A
AF014958	2.10971E-06	4.309E-06	1.05E-07	-0.42152	CCRL2
AF015553	2.10971E-06	9.536E-07	2.61E-07	0.61214	GTF2I
AF019083	1.37131E-05	5.009E-06	8.34E-07	0.17011	PTENP1
AF022375	2.63714E-07	8.227E-08	1.87E-11	-1.35847	VEGF
AF023614	1.37131E-05	1.511E-05	4.79E-07	-0.20744	TACI
AF024710	8.54758E-11	8.548E-11	1.13E-12	-1.95537	VEGF
AF026086	0.000344298	4.67E-05	2.66E-06	0.297942	PEX1
AF029777	1.37131E-05	7.048E-06	8.27E-07	0.290159	GCN5L2
AF030249	1.37131E-05	1.613E-06	1.98E-07	0.534547	ECH1
AF035281	2.10971E-06	2.484E-06	4.87E-07	0.472445	

AF038564	1.37131E-05	1.613E-06	2.05E-07	-0.40446	ITCH
AF040707	2.10971E-06	1.993E-06	3.57E-07	0.289845	NPR2L
AF042386	1.37131E-05	5.009E-06	0.000107	0.137192	PPIE
AF052160	7.44428E-05	1.511E-05	1.67E-06	0.623021	
AF054176	2.10971E-06	1.329E-07	6.47E-09	-0.58138	C1orf7
AF054589	0.000344298	2.35E-05	1.98E-06	0.945394	
AF061258	7.44428E-05	9.644E-05	1.58E-06	0.622201	LIM
AF067853	1.37131E-05	5.009E-06	5.02E-06	0.361707	ADSL
AF069517	2.10971E-06	1.329E-07	4.91E-07	0.399638	RBM6
AF070582	2.63714E-07	1.715E-07	3.23E-08	-0.19773	MGC13033
AF070606	1.37131E-05	3.06E-05	1.48E-06	-0.89337	
AF070617	1.37131E-05	3.861E-06	3.23E-07	0.323494	
AF077820	2.63714E-07	2.188E-08	2.91E-08	0.656852	LRP5
AF079167	2.63714E-07	2.488E-07	7.37E-10	-1.93249	OLR1
AF082557	0.00137719	4.67E-05	2.23E-06	0.226994	TNKS
AF094481	1.37131E-05	5.009E-06	2.74E-07	-0.29045	CGGBP1
AF098641	2.63714E-07	1.715E-07	1.56E-07	-0.41172	
AF110377	1.37131E-05	5.009E-06	3.05E-05	0.361232	TRRAP
AF117829	7.44428E-05	0.000129	2.61E-06	-0.57516	RIPK2
AI133727	7.44428E-05	0.0001187	1.43E-06	0.181464	FLB6421
AI141670	0.000344298	0.0003041	1.6E-06	-0.2494	CLCN2
AI148772	0.000344298	4.67E-05	4.18E-06	-1.02619	KYNU
AI184802	2.63714E-07	2.188E-08	2.67E-09	-0.21576	HPRP4P
AI560890	2.57282E-08	2.829E-08	1.8E-07	0.179028	
AI670100	7.44428E-05	2.577E-05	7.7E-07	0.22677	GRLF1
AI754391	1.37131E-05	3.861E-06	1.72E-06	-0.27657	KLF12
AI935146	0.000344298	2.35E-05	2.05E-06	-0.46726	GALNT3
AI950382	1.37131E-05	1.613E-06	1.63E-07	-0.74128	KIAA0585
AI970189	0.000344298	2.35E-05	6.16E-07	-0.75934	KIAA0997
AJ002190	7.44428E-05	1.613E-06	2.17E-08	0.33775	GNPAT
AJ007042	2.63714E-07	1.715E-07	2.1E-07	0.170935	WHSC1
AJ010059	2.10971E-06	5.045E-07	2.95E-06	0.2235	SIT
AL008583	2.63714E-07	2.188E-08	1.12E-08	0.250082	CBX6
AL021154	0.000344298	4.67E-05	2.19E-06	-0.82935	ID3
AL021707	0.000344298	7.048E-06	4.95E-06	-2.21462	
AL022398	7.44428E-05	1.613E-06	8.09E-08	0.919627	
AL022398	7.44428E-05	7.048E-06	1.1E-07	0.79713	DJ434O14.3
AL022398	7.44428E-05	2.577E-05	2.4E-06	0.493166	
AL023553	1.37131E-05	1.753E-05	2.51E-06	0.226635	PMM1
AL049387	0.00137719	0.0001897	5.12E-06	0.379296	
AL049409	7.44428E-05	1.511E-05	1.1E-06	0.714173	LEF1
AL049782	7.44428E-05	2.577E-05	7.66E-07	0.237794	
AL049787	1.37131E-05	5.009E-06	7.11E-06	0.311278	
AL049963	0.000344298	4.67E-05	8.36E-07	-0.74421	LOC64116
AL050084	7.44428E-05	1.613E-06	5.26E-05	0.509331	DC8
AL050087	2.10971E-06	2.484E-06	1.27E-07	-0.31279	KIAA1785
AL050196	1.37131E-05	5.009E-06	2E-05	-0.24688	DKFZP586D2223
AL050281	0.000344298	0.0002051	2.85E-06	0.30517	NAG
AL050353	0.000344298	2.35E-05	4.42E-06	0.179352	OIP2
AL050371	0.000344298	2.35E-05	3.7E-06	0.493288	PISD

AL080071	0.000344298	0.0003041	3.12E-06	0.237367	DKFZP564M082
AL080141	1.37131E-05	5.009E-06	2.42E-07	0.330868	SEC31B-1
AL096780	1.37131E-05	5.045E-07	2.13E-06	0.34487	CHKL
AW051579	1.37131E-05	1.613E-06	7.58E-07	0.593476	FLJ10512
D10704	1.37131E-05	1.753E-05	4.69E-07	-0.36791	CHK
D13891	2.10971E-06	2.484E-06	4.57E-05	-0.20577	ID2
D30758	2.10971E-06	1.993E-06	1.58E-05	0.27738	CENTB1
D30783	2.57282E-08	2.829E-08	8.95E-10	-1.65011	EREG
D49677	7.44428E-05	7.048E-06	4.18E-06	0.198707	U2AF1RS2
D50406	1.37131E-05	3.861E-06	2.65E-05	0.461907	RECK
D50525	0.000344298	4.67E-05	3.02E-06	0.486698	
D78579	1.37131E-05	7.048E-06	4.25E-07	-1.65638	NR4A3
D78579	7.44428E-05	7.048E-06	9.62E-07	-1.61438	NR4A3
D80011	7.44428E-05	1.613E-06	4.2E-07	-0.35073	KIAA0189
D87119	7.44428E-05	2.35E-05	1.8E-06	0.425625	GS3955
D87119	7.44428E-05	5.226E-05	4.62E-06	0.557116	GS3955
D87466	1.37131E-05	8.661E-06	1.49E-07	0.466046	KIAA0276
HG1103-HT1103	1.37131E-05	1.613E-06	1.16E-07	-0.39165	
HG2007-HT2056	7.44428E-05	9.644E-05	4.01E-06	-0.41408	
HG2724-HT2820	1.37131E-05	3.06E-05	5.17E-06	-1.33814	
HG3227-HT3404	2.63714E-07	1.715E-07	1.68E-08	-0.25361	
HG4582-HT4987	7.44428E-05	2.35E-05	4.63E-07	-0.39588	
J02939	7.44428E-05	1.613E-06	2.16E-07	-0.87844	SLC3A2
J02973	1.37131E-05	5.045E-07	2.93E-07	-1.30804	THBD
J03258	0.000344298	0.0001695	1.21E-06	-0.58295	VDR
J04130	0.000344298	2.35E-05	3.02E-06	-0.62071	SCYA4
L04733	0.00137719	2.35E-05	8.84E-07	0.306455	KNS2
L05424	2.10971E-06	1.329E-07	2.27E-09	-0.58081	CD44
L12002	7.44428E-05	4.67E-05	1.23E-06	0.286717	ITGA4
L13740	2.63714E-07	2.188E-08	5.83E-08	-1.45891	NR4A1
L13740	1.37131E-05	5.009E-06	9.1E-08	-0.61928	NR4A1
L13773	1.37131E-05	1.753E-05	6.44E-07	0.247919	MLLT2
L16499	1.37131E-05	8.661E-06	5.12E-06	0.374296	HHEX
L20941	2.63714E-07	1.329E-07	1.78E-06	-0.58618	FTH1
L22075	2.63714E-07	2.488E-07	1.1E-08	-0.55736	GNA13
L22569	1.37131E-05	8.661E-06	1.52E-06	0.318129	CTSB
L25665	0.000344298	0.0001695	3.34E-06	-0.4513	GNL1
L33881	2.63714E-07	1.715E-07	5.06E-08	-0.59585	PRKCI
L40377	1.37131E-05	5.045E-07	3.49E-07	-0.79409	SERPINB8
L47738	2.57282E-08	4.013E-09	7.54E-09	0.31646	PIR121
L78132	7.44428E-05	5.226E-05	5.15E-07	0.358576	LGALS8
M12267	0.000344298	0.0001695	4.07E-06	-0.3279	OAT
M12959	7.44428E-05	2.577E-05	1.61E-06	0.128482	TRA@
M15330	8.54758E-11	8.548E-11	2.49E-12	-2.13825	IL1B
M17017	7.44428E-05	0.0001187	1.43E-06	-1.74073	IL8
M22919	2.63714E-07	3.119E-07	9.52E-08	-0.81053	MYL6
M23114	2.10971E-06	4.309E-06	1.59E-07	-0.96141	ATP2A2
M24194	7.44428E-05	1.613E-06	4.38E-06	0.560895	GNB2L1
M24283	0.000344298	4.67E-05	3.71E-06	-1.32611	ICAM1
M24895	2.10971E-06	1.329E-07	1.72E-08	0.476779	AMY2B

M26683	7.44428E-05	0.0001187	3.7E-06	-0.16179	SCYA2
M27492	0.000344298	0.0004017	2.01E-06	-0.32619	IL1R1
M28130	7.44428E-05	4.67E-05	8.02E-07	-2.27292	IL8
M31165	7.44428E-05	5.226E-05	1.38E-06	-0.34617	TNFAIP6
M31523	1.37131E-05	1.753E-05	2.09E-06	0.36898	TCF3
M36821	1.37131E-05	8.661E-06	2.21E-07	-0.36334	GRO3
M55153	7.44428E-05	2.577E-05	4.77E-06	-0.27465	TGM2
M58603	7.44428E-05	5.226E-05	1.28E-06	-0.73537	NFKB1
M59040	0.00137719	2.35E-05	2.82E-06	-0.46271	CD44
M60784	7.44428E-05	5.226E-05	1.24E-06	0.559903	SNRPA
M60922	7.44428E-05	1.511E-05	4.47E-08	0.39657	FLOT2
M62403	7.44428E-05	5.226E-05	5.57E-07	-0.53749	IGFBP4
M63256	0.000344298	5.915E-05	6.54E-07	0.454561	CDR2
M63904	2.57282E-08	1.031E-08	5.38E-09	-0.59612	GNA15
M63978	0.000344298	4.67E-05	1.77E-06	-0.44762	VEGF
M64571	1.83773E-09	1.838E-09	2.41E-11	0.416659	MAP4
M69199	2.10971E-06	1.993E-06	1.45E-07	-1.9021	G0S2
M73547	1.37131E-05	5.009E-06	9.2E-08	0.438897	D5S346
M74525	2.10971E-06	2.484E-06	3.5E-07	-0.61792	UBE2B
M80244	0.000344298	7.048E-06	2.72E-06	-0.8522	SLC7A5
M84443	1.37131E-05	5.045E-07	4.08E-07	0.303567	GALK2
M94856	7.44428E-05	5.226E-05	4.99E-06	-0.23847	FABP5
M95678	0.000344298	7.048E-06	2E-06	0.432923	PLCB2
M98833	7.44428E-05	1.613E-06	1.52E-06	0.434288	FLI1
N23137	2.10971E-06	2.484E-06	2.06E-07	0.247311	MPHOSPH9
N23137	0.00137719	0.0001695	4.12E-06	0.244083	MPHOSPH9
N30151	7.44428E-05	1.613E-06	5.05E-05	0.393521	STX16
N42007	2.10971E-06	2.484E-06	9.19E-05	0.167986	NUP50
N53547	7.44428E-05	8.556E-05	1.8E-07	0.296678	MGC5508
N90862	1.37131E-05	5.045E-07	3.28E-08	0.43576	VAMP8
N90866	2.63714E-07	8.227E-08	2.76E-08	0.304525	CDW52
N98667	1.37131E-05	8.661E-06	3.38E-07	0.367127	KIAA1696
R90942	1.37131E-05	5.009E-06	1.05E-05	-0.17696	ST6GALNACIV
S52028	2.10971E-06	5.045E-07	9.62E-08	-0.81662	CTH
S68134	0.000344298	7.048E-06	8.37E-07	-1.64652	CREM
S68134	0.000344298	7.048E-06	4.35E-06	-2.47105	CREM
S68271	0.000344298	7.048E-06	3.03E-06	-2.07185	CREM
S73591	1.37131E-05	1.511E-05	4.68E-06	0.414777	VDUP1
S76638	7.44428E-05	2.35E-05	7.47E-07	-0.35416	NFKB2
S78187	7.44428E-05	1.613E-06	1.95E-05	0.203265	CDC25B
S78771	0.000344298	5.915E-05	2.55E-06	-0.31389	BRD2
S81914	0.000344298	7.048E-06	4.18E-07	-1.59146	IER3
U02020	1.37131E-05	8.661E-06	1.37E-06	-1.13863	PBEF
U02570	1.37131E-05	2.813E-05	1.26E-06	0.432431	ARHGAP1
U03634	1.37131E-05	1.753E-05	1E-06	-0.21467	LBC
U04636	0.000344298	5.915E-05	2.81E-06	-1.85123	PTGS2
U05681	7.44428E-05	5.226E-05	3.37E-06	-0.35383	BCL3
U07563	7.44428E-05	2.35E-05	4.91E-07	-0.25016	ABL1
U09937	1.83773E-09	4.157E-10	2.04E-09	-1.21578	PLAUR
U10117	7.44428E-05	1.511E-05	4.07E-06	0.563673	SCYE1

U11732	1.37131E-05	3.861E-06	3.04E-07	-0.22574	ETV6
U12767	7.44428E-05	1.613E-06	2.84E-07	-1.23483	NR4A3
U12767	0.000344298	7.048E-06	2.55E-07	-2.13744	NR4A3
U13695	7.44428E-05	1.613E-06	1.11E-05	0.805607	PMS1
U15552	1.37131E-05	5.009E-06	1.67E-05	-0.68094	HSU15552
U17760	0.000344298	7.048E-06	4.25E-06	-0.84472	LAMB3
U18300	7.44428E-05	0.000129	2.43E-06	0.183171	DDB2
U20982	2.10971E-06	1.993E-06	1.2E-08	-0.67125	IGFBP4
U24166	7.44428E-05	1.613E-06	7.52E-06	-0.45293	MAPRE1
U28811	0.000344298	7.048E-06	1.33E-06	0.32855	GLG1
U29171	1.37131E-05	5.009E-06	1.1E-06	-0.6032	CSNK1D
U29175	1.37131E-05	8.661E-06	1.9E-06	0.266342	SMARCA4
U29185	2.10971E-06	7.732E-07	1.56E-07	-1.08006	PRNP
U29344	2.10971E-06	9.536E-07	2.35E-07	-0.43842	FASN
U29656	2.10971E-06	7.732E-07	7.52E-08	0.353186	NME3
U29656	7.44428E-05	0.000129	4.31E-06	0.471876	NME3
U32324	1.37131E-05	5.045E-07	3.21E-08	0.334966	IL11RA
U33017	2.63714E-07	1.715E-07	5.2E-07	0.373581	SLAM
U38847	7.44428E-05	2.35E-05	9.91E-07	0.222946	TARBP1
U41815	1.37131E-05	5.045E-07	2.16E-07	-0.96931	NUP98
U43774	0.000344298	2.35E-05	8.8E-07	-0.39938	FCAR
U44839	2.10971E-06	9.536E-07	2.54E-07	-0.97008	USP11
U47414	2.10971E-06	9.536E-07	2.31E-06	0.370736	CCNG2
U47927	2.57282E-08	2.829E-08	5.53E-09	0.545592	USP5
U48807	1.37131E-05	5.009E-06	4.97E-08	-0.93178	DUSP4
U49187	7.44428E-05	1.511E-05	1.48E-06	0.671467	C6orf32
U49187	7.44428E-05	9.644E-05	3.53E-06	0.511392	C6orf32
U49844	7.44428E-05	7.048E-06	3.67E-07	0.47168	ATR
U50527	1.37131E-05	5.009E-06	5.11E-06	0.416543	
U50928	7.44428E-05	1.613E-06	4.72E-06	0.302213	PKD2
U51007	7.44428E-05	1.511E-05	1.49E-06	0.309996	PSMD4
U51205	1.37131E-05	5.045E-07	2.65E-07	-0.76279	COP9
U51478	7.44428E-05	2.35E-05	6.1E-07	-0.58	ATP1B3
U51920	2.10971E-06	1.329E-07	7.01E-08	-0.28142	SRP54
U52960	2.10971E-06	1.613E-06	1.51E-07	-0.84863	SURB7
U56998	0.000344298	7.048E-06	3.7E-06	-0.74294	CNK
U64197	1.83773E-09	1.838E-09	2.95E-10	-0.62373	SCYA20
U65928	7.44428E-05	4.67E-05	2.85E-07	0.408918	COPS5
U66063	2.10971E-06	2.484E-06	4.7E-07	0.277185	CAMK2G
U70735	1.37131E-05	8.661E-06	1.82E-06	0.249185	MOV34-34KD
U72066	2.57282E-08	1.031E-08	4.33E-08	-0.34482	RBBP8
U75968	2.10971E-06	1.993E-06	4.36E-06	0.139542	DDX11
U78107	8.54758E-11	3.691E-11	4.04E-12	-0.43769	NAPG
U78302	2.63714E-07	1.715E-07	2.41E-08	0.329878	DECR1
U78798	2.57282E-08	4.013E-09	1.11E-06	-0.3172	TRAF6
U84007	7.44428E-05	1.613E-06	0.000235	0.236422	AGL
U85245	7.44428E-05	1.613E-06	4.57E-07	0.365266	PIP5K2B
U88629	0.000344298	4.67E-05	9.58E-07	-0.32607	ELL2
U90917	1.37131E-05	1.613E-06	3.89E-07	0.433406	FOXM1
U91543	2.63714E-07	3.119E-07	2.01E-07	0.478678	CHD3

U91616	1.37131E-05	5.045E-07	1.27E-07	-0.80419	NFKBIE
U96876	7.44428E-05	1.613E-06	3.54E-06	-0.45317	INSIG1
U97105	1.37131E-05	1.753E-05	6.56E-07	1.00615	DPYSL2
W28319	1.37131E-05	5.009E-06	1.5E-05	0.294631	FBLN1
W28612	1.37131E-05	5.009E-06	1.7E-06	-0.25519	
W28743	0.000344298	7.048E-06	2.78E-06	-0.28926	PP1628
X00737	2.10971E-06	9.536E-07	5.21E-08	-0.67074	NP
X02152	1.37131E-05	5.045E-07	4.63E-08	-0.75601	LDHA
X04366	1.37131E-05	2.813E-05	5.11E-06	0.346076	CAPN1
X04500	2.63714E-07	1.715E-07	3.43E-10	-2.12121	IL1B
X06256	1.37131E-05	2.35E-05	4.89E-07	-0.7357	ITGA5
X13403	7.44428E-05	5.915E-05	4.21E-07	0.146032	POU2F1
X15217	7.44428E-05	4.67E-05	3.77E-07	-0.2371	SKIL
X15218	8.54758E-11	8.548E-11	1.4E-10	-1.41501	SKI
X16396	0.000344298	0.0002051	3.27E-06	-0.6151	MTHFD2
X16706	7.44428E-05	1.613E-06	1.23E-06	-1.09747	FOSL2
X53586	1.37131E-05	8.661E-06	3.4E-07	0.51291	ITGA6
X58141	7.44428E-05	9.644E-05	1.75E-06	0.384254	ADD1
X61123	7.44428E-05	0.0001057	4.17E-07	-1.15256	BTG1
X61498	7.44428E-05	1.613E-06	8.8E-07	-0.49884	NFKB2
X62535	1.37131E-05	1.613E-06	5.68E-07	0.243937	DGKA
X63368	2.10971E-06	5.045E-07	2.3E-08	-0.55432	DNAJB2
X64330	7.44428E-05	7.048E-06	2.27E-06	0.297851	ACLY
X66363	2.63714E-07	1.715E-07	6.53E-07	-0.24505	PCTK1
X66436	0.000344298	8.556E-05	1.88E-06	-0.26662	
X66945	7.44428E-05	1.511E-05	1.91E-07	-0.35494	FGFR1
X68452	2.57282E-08	4.013E-09	9.12E-11	-0.26618	CCND2
X69392	2.63714E-07	1.329E-07	1.1E-08	0.297444	RPL26
X70218	1.37131E-05	3.06E-05	2.44E-06	-0.74691	PPP4C
X74039	1.83773E-09	4.157E-10	1.51E-10	-0.67381	PLAUR
X79882	1.37131E-05	5.045E-07	1.78E-07	0.520965	MVP
X82153	7.44428E-05	1.613E-06	2.27E-06	0.47844	CTSK
X82209	2.10971E-06	5.045E-07	1.37E-09	-0.45281	MN1
X87949	7.44428E-05	1.613E-06	4.05E-07	-0.54468	HSPA5
X98172	7.44428E-05	4.67E-05	5.29E-07	0.507556	CASP8
X99142	1.37131E-05	8.661E-06	1.24E-06	-0.29773	KRTHB6
X99656	1.37131E-05	5.045E-07	1.68E-06	-0.23553	SH3GL1
Y00630	2.57282E-08	3.695E-08	6.65E-09	-2.38485	SERPINB2
Y08683	1.37131E-05	5.045E-07	4.71E-06	0.492738	CPT1B
Y14768	1.37131E-05	5.045E-07	7.26E-08	0.248383	LTB
Y18004	1.37131E-05	5.009E-06	4.19E-07	-0.9465	SCML2
Z11697	1.37131E-05	5.045E-07	3.55E-06	-1.21033	CD83
Z14000	0.000344298	0.0002051	3.91E-06	-0.33734	RING1
Z24724	2.63714E-07	2.188E-08	5.96E-09	-1.10426	
Z32860	1.37131E-05	5.009E-06	7.81E-06	0.133192	
Z93930	2.63714E-07	2.488E-07	2.42E-05	-0.39839	XBP1

Table III: Differential Gene Expression in acute MS relapse vs. remission

Identifier	TNOM PValue	Info PValue	t-Test PValue	Log Fold Change	Symbol
AI828210	5.38E-06	5.38E-06	8.37E-06	-0.18947	KIAA0284
D14710	6.73E-05	3.19E-05	2.89E-05	-0.35496	ATP5A1
U46692	6.73E-05	3.19E-05	0.000284	-0.49741	CSTB
AF061261	6.73E-05	3.19E-05	3.22E-05	-0.28274	MBLL
U51712	6.73E-05	3.19E-05	0.003464	-0.42775	SMAP31
AB014558	6.73E-05	4.25E-05	0.000473	0.694784	CRY2
AB007936	6.73E-05	4.25E-05	0.000958	-0.25409	KIAA0467
AC002115	6.73E-05	4.25E-05	0.000147	0.622841	MGC10433
AF052160	6.73E-05	4.25E-05	0.000182	-0.46468	
S78085	0.000538	0.000104	0.000102	-0.55064	PDCD2
AL096719	0.000538	0.000104	0.000089	-0.22287	PFN2
U61234	0.000538	0.000104	0.000844	0.299182	TBCC
X12451	0.000538	0.000251	0.000876	1.04444	CTSL
M35531	0.000538	0.000251	0.000241	-0.20303	FUT1
M64174	0.000538	0.000251	3.43E-05	-0.5508	JAK1
AB018269	0.000538	0.000251	7.39E-05	-0.18186	KIAA0726
R92331	0.000538	0.000251	0.000104	0.289994	MT1E
U19487	0.000538	0.000251	0.001738	-0.25888	PTGER2
AF040965	0.000538	0.000251	0.000775	0.48898	RES4-25
U07563	0.000538	0.000251	3.61E-05	-0.16779	RRP4
L40377	0.000538	0.000251	0.009479	0.452416	SERPINB8
AL080234	0.000538	0.000251	0.000377	-0.52631	
AJ242015	0.003096	0.00039	0.013957	0.281618	ADAM28
D86324	0.003096	0.00039	0.001801	-0.34728	CMAH
M94065	0.003096	0.00039	0.002391	-0.13976	DHODH
AC004382	0.003096	0.00039	0.000121	-0.20383	DKFZP434K046
X54326	0.003096	0.00039	0.002734	-0.39559	EPRS
W25921	0.003096	0.00039	9.41E-05	-0.39027	GNS
X92110	0.003096	0.00039	0.000103	-1.00581	HCGVIII-1
W28589	0.003096	0.00039	0.000225	-0.20949	HSPD1
S66213	0.003096	0.00039	0.000134	-0.28606	ITGA6
AB011158	0.000538	0.00039	0.000047	-0.163	KIAA0586
AB023209	0.003096	0.00039	0.003354	-0.09151	KIAA0992
AF035940	0.003096	0.00039	0.008457	0.282437	MAGOH
M31724	0.003096	0.00039	0.000671	0.569343	PTPN1
X74262	0.003096	0.00039	0.000062	-0.37623	RBBP4
J05249	0.003096	0.00039	0.00045	-0.52346	RPA2
M55531	0.003096	0.00039	0.023054	-0.22329	SLC2A5
AI865431	0.003096	0.00039	0.00027	0.423067	TNFRSF5
W28203	0.003096	0.00039	0.007983	-0.17484	
W28667	0.003096	0.00039	0.000846	-0.49488	
D13628	0.000538	0.000529	0.034335	-0.10398	ANGPT1
U03271	0.000538	0.000529	0.000286	-0.1675	CAPZB
U05259	0.000538	0.000529	0.003589	0.551328	CD79A
L13278	0.000538	0.000529	7.27E-05	-0.43636	CRYZ
M91670	0.000538	0.000529	0.003472	0.600255	E2-EPF
AB029030	0.000538	0.000529	0.000657	-0.13458	KIAA1107
AF016098	0.000538	0.000529	0.000433	-0.16189	NRP2

X76091	0.000538	0.000529	0.004691	0.161349	RFX2
U52191	0.000538	0.000529	0.00229	1.2356	SMCY
AA203345	0.000538	0.000529	0.001228	-0.50409	STX16
U96113	0.000538	0.000529	0.000394	-0.41425	WWP1
AL050263	0.000538	0.000529	0.000224	-0.15981	
Z48579	0.000538	0.000799	0.000184	-0.30836	ADAM10
M31452	0.000538	0.000799	0.002899	-0.13022	C4BPA
AC003107	0.000538	0.000799	0.000262	-0.16818	COMP
M91670	0.000538	0.000799	0.000792	0.41925	E2-EPF
AB023235	0.000538	0.000799	0.001348	-0.30138	KIAA1018
X89960	0.000538	0.000799	0.026837	-0.35169	MCSP
D55654	0.000538	0.000799	0.019331	-0.2254	MDH1
U02683	0.000538	0.000799	0.030035	-0.09324	NRF1
S90469	0.000538	0.000799	0.000785	0.23032	POR
AF020543	0.000538	0.000799	0.004286	-0.25061	PPT2
M34181	0.000538	0.000799	0.000055	-0.5883	PRKACB
AF095448	0.000538	0.000799	0.000588	-0.24961	RAI3
AF027150	0.000538	0.000799	0.000979	-0.16012	SIP1
X02344	0.000538	0.000799	0.000918	0.430531	TUBB2
X02344	0.000538	0.000799	0.002225	0.296682	TUBB2
AI701164	0.000538	0.000799	0.000115	-0.23639	UBE2G1
U96113	0.000538	0.000799	9.77E-05	-0.45711	WWP1
AF016052	0.000538	0.000799	0.001254	-0.19092	ZNF24
U21551	0.003096	0.00103	0.000836	0.278219	BCAT1
X77794	0.003096	0.00103	3.72E-05	-0.81938	CCNG1
AF070530	0.003096	0.00103	0.014908	0.276942	CL24751
AB002331	0.003096	0.00103	0.001714	-0.17304	DATF1
AI004207	0.003096	0.00103	0.000762	-0.1648	FLJ00002
L76200	0.003096	0.00103	0.000824	0.444479	GUK1
U26398	0.003096	0.00103	0.001182	-0.29185	INPP4A
U69883	0.003096	0.00103	0.007922	0.103614	KCNN1
M13452	0.003096	0.00103	0.000467	0.405856	LMNA
AA126505	0.003096	0.00103	0.002	-0.39781	NCAM1
U88620	0.003096	0.00103	0.007562	-0.3532	OGG1
M33336	0.003096	0.00103	0.001568	-0.26454	PRKAR1A
AB015982	0.003096	0.00103	0.000382	-0.27486	PRKCN
H68340	0.003096	0.00103	0.001222	0.516352	RNAHP
M28225	0.003096	0.00103	0.000686	1.0733	SCYA2
X97064	0.003096	0.00103	0.003207	-0.19906	SEC23A
X68560	0.003096	0.00103	0.007856	0.437567	SP3
AF064094	0.003096	0.00103	0.000287	-0.19385	TADA2L
AB007872	0.003096	0.00103	0.000119	-0.20778	ZNF264
W28255	0.013622	0.001698	0.001407	-0.24426	76P
AB007934	0.003096	0.001698	0.003182	-0.24405	ACF7
AL049954	0.013622	0.001698	0.024193	-0.25818	AHCYL1
U90546	0.003096	0.001698	0.000105	-0.34074	BTN3A2
AL035291	0.013622	0.001698	0.007668	0.506107	CH1
AF031647	0.013622	0.001698	0.004755	0.257244	COPS3
M57888	0.003096	0.001698	0.004549	-0.64384	CTLA1
AF000987	0.003096	0.001698	0.009455	0.247586	EIF1AY

U55766	0.003096	0.001698	0.00066	0.795017	HRB2
L12002	0.013622	0.001698	0.005765	-0.1942	ITGA4
D14661	0.013622	0.001698	0.011324	0.391267	KIAA0105
D63875	0.013622	0.001698	0.002192	-0.36411	KIAA0155
AB018285	0.013622	0.001698	0.001545	0.550994	KIAA0742
AB023180	0.013622	0.001698	0.001642	0.253479	KIAA0963
AL080102	0.013622	0.001698	0.003651	0.435751	KIAA1856
M22637	0.013622	0.001698	0.003792	-0.27794	LYL1
D85131	0.013622	0.001698	0.005126	-0.12291	MAZ
D37965	0.013622	0.001698	0.01111	-0.09143	PDGFRL
Y18207	0.003096	0.001698	0.003474	-0.17238	PPP1R3C
L49229	0.013622	0.001698	0.000336	-0.36639	RB1
U77664	0.013622	0.001698	0.002354	0.193666	RPP38
AL040137	0.003096	0.001698	0.008384	-0.23366	SAP18
D31764	0.013622	0.001698	0.01295	-0.13299	SNX17
X57655	0.013622	0.001698	0.002476	-0.17382	SPINK2
M19267	0.013622	0.001698	0.013582	0.262886	TPM1
M12959	0.013622	0.001698	0.003907	-0.08942	TRA@
AA160724	0.013622	0.001698	0.005695	0.267002	
U37122	0.003096	0.002135	0.000571	-0.59281	ADD3
AA903720	0.003096	0.002135	0.002557	0.244618	BAP29
M93107	0.003096	0.002135	0.00187	-0.19146	BDH
M17754	0.003096	0.002135	0.010333	-0.10769	BN51T
X15882	0.003096	0.002135	0.0023	0.227769	COL6A2
D15057	0.003096	0.002135	0.002814	-0.26776	DAD1
S62138	0.003096	0.002135	0.002442	1.1158	DDIT3
AB026436	0.003096	0.002135	0.011189	0.711919	DUSP10
W27152	0.003096	0.002135	0.009498	-0.1614	FLJ10569
AB001106	0.003096	0.002135	0.002408	0.444617	GMFB
D87120	0.003096	0.002135	0.00475	0.236706	GS3786
AI200373	0.003096	0.002135	0.003822	-0.31066	H2AFI
U15085	0.003096	0.002135	0.011743	0.328857	HLA-DMB
U90549	0.003096	0.002135	0.001654	-0.26437	HMG17L3
AI760162	0.003096	0.002135	0.001313	-0.47775	HT012
AB018306	0.003096	0.002135	0.000371	0.316202	KIAA0763
D14696	0.003096	0.002135	0.016949	0.259239	LAPTM4A
U23852	0.003096	0.002135	0.001207	-0.2593	LCK
U70735	0.003096	0.002135	0.0002	-0.20846	MOV34-34KD
X79865	0.003096	0.002135	0.0141	0.418466	MRPL12
AI547258	0.003096	0.002135	0.001223	0.267951	MT2A
L40387	0.003096	0.002135	0.00038	0.211973	OASL
AB019517	0.003096	0.002135	0.023004	0.219453	PKIG
M58459	0.003096	0.002135	0.001362	1.46854	RPS4Y
X57348	0.003096	0.002135	0.004255	0.22047	SFN
M74558	0.003096	0.002135	0.001205	0.219185	SIL
U34044	0.003096	0.002135	0.000831	-0.21289	SPS
U49928	0.003096	0.002135	0.000886	-0.31189	TAB1
X05839	0.003096	0.002135	0.008747	0.214552	TGFB1
U16296	0.003096	0.002135	0.006585	-0.14857	TIAM1
U63127	0.003096	0.002135	0.000538	-0.38925	TIC

U03397	0.003096	0.002135	0.005156	-0.34157	TNFRSF9
M21624	0.003096	0.002135	0.001748	-0.51878	TRD@
D83198	0.003096	0.002135	0.028975	-0.17519	YF13H12
HG960-HT960	0.003096	0.002135	0.003089	0.145701	
HG4724-HT5166	0.003096	0.002135	0.002446	-0.25728	
D00654	0.003096	0.004342	9.79E-05	-0.1819	ACTG2
U54645	0.013622	0.004342	0.004228	-0.25281	AK2
M93405	0.003096	0.004342	0.020651	0.126156	ALDH6A1
U73960	0.003096	0.004342	0.002279	0.555806	ARL4
U26455	0.003096	0.004342	0.006562	-0.53911	ATM
M33519	0.003096	0.004342	0.011169	-0.33327	BAT3
U90028	0.003096	0.004342	0.000396	-0.24971	BICD1
AB002384	0.003096	0.004342	0.002855	-0.46941	C6orf32
M74093	0.003096	0.004342	0.000763	-0.33022	CCNE1
AA203246	0.003096	0.004342	0.007014	-0.16607	CDC2L5
X66358	0.013622	0.004342	0.007122	-0.1886	CDKL1
U30872	0.003096	0.004342	0.001715	-0.164	CENPF
AB020675	0.013622	0.004342	0.002913	-0.25056	CNTNAP2
M13207	0.013622	0.004342	0.01388	0.122241	CSF2
AA173896	0.013622	0.004342	0.008401	0.305133	CYB5-M
L78267	0.003096	0.004342	0.04708	0.103949	D15S226E
AL080120	0.013622	0.004342	0.001834	-0.12922	DKFZP564O0423
U13896	0.013622	0.004342	0.020482	-0.10291	DLG1
AF034970	0.013622	0.004342	0.010371	-0.10568	DOK2
D12686	0.013622	0.004342	0.003493	0.170378	EIF4G1
AB002386	0.003096	0.004342	0.000131	-0.39255	EZH1
M15059	0.003096	0.004342	0.002497	0.2061	FCER2
W27545	0.013622	0.004342	0.004445	0.379682	FLJ20259
M84443	0.003096	0.004342	0.000101	-0.27085	GALK2
AF029777	0.013622	0.004342	0.001427	-0.22426	GCN5L2
D63876	0.013622	0.004342	0.002737	0.396946	GGA3
AB020645	0.003096	0.004342	0.003907	-0.37377	GLS
U77948	0.003096	0.004342	0.000818	-0.35677	GTF2I
AF035555	0.003096	0.004342	0.018388	-0.17666	HADH2
AF055001	0.003096	0.004342	0.010744	0.724714	HERPUD1
D32129	0.003096	0.004342	0.005364	-0.13287	HLA-A
AF043586	0.003096	0.004342	0.001047	-0.30021	IGL@
U53831	0.013622	0.004342	0.01853	0.488267	IRF7
AB002344	0.003096	0.004342	0.001658	0.705775	KIAA0346
AI677689	0.013622	0.004342	0.004375	-0.1411	KIAA0685
AB023153	0.003096	0.004342	0.04282	-0.39134	KIAA0936
AB023226	0.003096	0.004342	0.000111	-0.71413	KIAA1009
AI148772	0.013622	0.004342	0.03739	0.532454	KYNU
AB006780	0.003096	0.004342	0.010236	0.178362	LGALS3
AL050405	0.003096	0.004342	0.008144	0.311843	LOC51634
L35253	0.013622	0.004342	0.001324	-0.46397	MAPK14
R93527	0.013622	0.004342	0.000372	0.264207	MT1H
AF108145	0.003096	0.004342	0.001206	-0.14877	MYLE
M96980	0.013622	0.004342	0.002106	-0.16409	MYT1

S76638	0.013622	0.004342	0.04529	0.171344	NFKB2
D88674	0.013622	0.004342	0.045232	0.346415	OAZIN
AL050353	0.013622	0.004342	0.016071	-0.11979	OIP2
AL080119	0.003096	0.004342	0.001961	-0.40821	PAI-RBP1
X76770	0.013622	0.004342	0.005011	-0.10613	PAPOLA
D11466	0.003096	0.004342	0.009752	0.738127	PIGA
W28299	0.003096	0.004342	0.001225	-0.17755	PINK1
U83981	0.003096	0.004342	0.014327	0.28747	PPP1R15A
X14968	0.013622	0.004342	0.004727	0.105215	PRKAR2A
M55284	0.003096	0.004342	0.003435	-0.17401	PRKCH
M15036	0.003096	0.004342	0.010965	-0.25119	PROS1
Y00638	0.003096	0.004342	0.004977	-0.30956	PTPRC
Y00815	0.003096	0.004342	0.015344	0.116938	PTPRF
M38258	0.003096	0.004342	0.009252	-0.14193	RARG
AF025654	0.003096	0.004342	0.002302	-0.39122	RNGTT
M60724	0.013622	0.004342	0.004732	-0.22065	RPS6KB1
AB006202	0.013622	0.004342	0.003028	-0.18268	SDHD
AA890010	0.003096	0.004342	0.00546	-0.21285	SEC22L1
X62822	0.003096	0.004342	0.039707	-0.21593	SIAT1
L41680	0.003096	0.004342	0.001771	-0.16486	SIAT8D
X15217	0.003096	0.004342	0.007377	0.149306	SKIL
L13857	0.003096	0.004342	0.005721	-0.11073	SOS1
U09564	0.003096	0.004342	0.001203	-0.27717	SRPK1
Z75330	0.013622	0.004342	0.031796	-0.11359	STAG1
X92762	0.003096	0.004342	0.001021	-0.27946	TAZ
AF064090	0.003096	0.004342	0.006206	0.303013	TNFSF14
U47634	0.003096	0.004342	0.0057	0.278205	TUBB4
L27071	0.003096	0.004342	0.000732	-0.39906	TXK
D78514	0.003096	0.004342	0.000681	-0.2599	UBE2G1
AF085807	0.003096	0.004342	0.005801	0.124457	UPK1A
U66561	0.003096	0.004342	0.002542	0.448044	ZNF184
X78925	0.013622	0.004342	0.001898	0.351929	ZNF267
HG2510-HT2606	0.013622	0.004342	0.007016	0.179499	
W27419	0.003096	0.004342	0.006325	0.341787	
AF054589	0.003096	0.004342	0.030568	-0.50762	
H98552	0.003096	0.004342	0.017185	-0.1057	
AI056697	0.003096	0.004342	0.000329	-0.20147	
X00351	0.003096	0.005207	0.001506	-0.12928	ACTB
AF006082	0.003096	0.005207	0.002797	-0.34587	ACTR2
Y09443	0.003096	0.005207	0.002286	-0.17646	AGPS
U22961	0.003096	0.005207	0.003092	0.147932	ALB
AF002163	0.003096	0.005207	0.002447	-0.37588	AP3D1
D87461	0.003096	0.005207	0.004809	-0.26338	BCL2L2
AF013759	0.003096	0.005207	0.004946	-0.18574	CALU
L22005	0.003096	0.005207	0.006442	0.131869	CDC34
AL109689	0.003096	0.005207	0.013291	-0.24945	CGI-142
U91543	0.003096	0.005207	0.014143	-0.25258	CHD3
X82153	0.003096	0.005207	0.013882	-0.31742	CTSK
AJ001687	0.003096	0.005207	0.000224	-0.64837	D12S2489E
M13149	0.003096	0.005207	0.008717	-0.13824	HRG

Y10313	0.003096	0.005207	0.006846	0.464769	IFRD1
D63485	0.003096	0.005207	0.000985	-0.31599	IKKE
D87077	0.003096	0.005207	0.043072	-0.21138	KIAA0240
AB007864	0.003096	0.005207	0.001569	0.256672	KIAA0404
X75346	0.003096	0.005207	0.001841	0.331699	MAPKAPK2
L07648	0.003096	0.005207	0.010594	0.226817	MXI1
AB028993	0.003096	0.005207	0.0247	0.133216	NLGN1
D45333	0.003096	0.005207	0.002104	0.302454	PFDN1
M65254	0.003096	0.005207	0.002619	0.262897	PPP2R1B
M86852	0.003096	0.005207	0.004274	0.172251	PXMP3
X97795	0.003096	0.005207	0.021131	-0.18349	RAD54L
U14970	0.003096	0.005207	0.001894	-0.1353	RPS5
X74570	0.003096	0.005207	0.00345	0.210049	SIAT4C
X98248	0.003096	0.005207	0.010403	-0.50617	SORT1
U17714	0.003096	0.005207	0.002081	-0.19372	ST13
W28869	0.003096	0.005207	0.001369	-0.38498	TEGT
M12125	0.003096	0.005207	0.000178	-0.09929	TPM2
L27071	0.003096	0.005207	0.003834	-0.36074	TXK
M60614	0.003096	0.005207	0.001757	-0.25283	WIT-1
HG4074-HT4344	0.003096	0.005207	0.004175	0.589048	
AL031846	0.003096	0.005207	0.004012	-0.42132	
HG1980-HT2023	0.003096	0.005207	0.002314	0.711234	
AF022853	0.047678	0.006683	0.002056	-0.30792	ABCC1
X02994	0.047678	0.006683	0.036598	-0.12393	ADA
D25304	0.047678	0.006683	0.002258	-0.44746	ARHGEF6
M23115	0.047678	0.006683	0.016518	-0.1243	ATP2A2
U87408	0.047678	0.006683	0.008628	-0.33961	B1
AA135683	0.047678	0.006683	0.010045	0.6329	BASP1
M22491	0.047678	0.006683	0.020141	-0.10386	BMP3
M28170	0.047678	0.006683	0.014303	0.280093	CD19
M16336	0.047678	0.006683	0.011755	-0.19993	CD2
U37022	0.047678	0.006683	0.028135	-0.06885	CDK4
U66469	0.047678	0.006683	0.004123	0.616896	CGR19
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J03071	0.047678	0.006683	0.011153	-0.23776	CSH2
M55265	0.047678	0.006683	0.01278	-0.1479	CSNK2A1
M33317	0.047678	0.006683	0.014832	-0.17753	CYP2A7
U37143	0.013622	0.006683	0.001908	0.171138	CYP2J2
AL049942	0.013622	0.006683	0.00076	-0.20245	DKFZP564F1422
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L35594	0.013622	0.006683	0.002806	0.216985	ENPP2
J03796	0.047678	0.006683	0.002596	-0.28198	EPB41
AC002398	0.013622	0.006683	0.003226	-0.27062	F25965
X15376	0.013622	0.006683	0.014388	-0.15607	GABRG2
M90656	0.047678	0.006683	0.006961	-0.15968	GCLC
AF062006	0.013622	0.006683	0.001442	0.200117	GPR49
X61755	0.013622	0.006683	0.000491	-0.19331	HOXC5
D21851	0.047678	0.006683	0.017915	0.153927	KIAA0028
AB007976	0.047678	0.006683	0.032427	0.228873	KIAA0507

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AB020660	0.047678	0.006683	0.001858	-0.27616	KIAA0853
X93595	0.047678	0.006683	0.026214	0.245064	KIR3DL2
AB002405	0.047678	0.006683	0.003681	-0.19481	LAK-4P
X07228	0.047678	0.006683	0.046458	0.113484	LIPC
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U59423	0.047678	0.006683	0.01126	-0.1341	MADH1
U85430	0.013622	0.006683	0.000224	-0.41454	NFATC3
X80878	0.047678	0.006683	0.010021	-0.16096	NFRKB
AF005043	0.013622	0.006683	0.00078	-0.15296	PARG
D49818	0.047678	0.006683	0.021976	-0.10631	PFKFB4
M28393	0.013622	0.006683	0.003241	-0.16419	PRF1
Y00062	0.047678	0.006683	0.011868	-0.2415	PTPRC
L07758	0.047678	0.006683	0.008943	0.201883	PWP1
U57094	0.047678	0.006683	0.014944	-0.31108	RAB27A
M35416	0.013622	0.006683	0.002789	-0.41233	RALB
X75042	0.047678	0.006683	0.003614	0.659166	REL
AF038250	0.047678	0.006683	0.004198	0.395171	SFRS3
L27213	0.013622	0.006683	0.001014	-0.13065	SLC4A3
Y09568	0.047678	0.006683	0.005799	-0.3407	SNAP23
AA205857	0.013622	0.006683	0.00048	0.27495	SNRPD3
U07794	0.047678	0.006683	0.007632	-0.20733	TXK
J05428	0.013622	0.006683	0.00573	-0.08342	UGT2B7
U09848	0.047678	0.006683	0.011538	-0.26846	ZNF36
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AB004066	0.013622	0.009369	0.00789	0.494455	BHLHB2
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AB024704	0.013622	0.009369	0.010893	-0.11914	C20orf1
AC004084	0.013622	0.009369	0.005491	-0.17437	CAPRI
L12691	0.013622	0.009369	0.018291	-0.18848	DEFA3
L19161	0.013622	0.009369	0.001645	-0.27253	EIF2S3
M82882	0.013622	0.009369	0.003966	0.478256	ELF1
X81625	0.013622	0.009369	0.003918	0.762544	ETF1
M15059	0.013622	0.009369	0.035106	0.313247	FCER2
AA284298	0.013622	0.009369	0.028745	-0.12535	FLJ22269
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X75315	0.013622	0.009369	0.002959	1.06191	HSRNASEB
AF064084	0.013622	0.009369	0.017927	-0.10308	ICMT
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AB014569	0.013622	0.009369	0.010011	0.709572	KIAA0669
AI970189	0.013622	0.009369	0.001778	0.569801	KIAA0997
AB028960	0.013622	0.009369	0.001825	-0.15403	KIAA1037
AJ005273	0.013622	0.009369	0.001449	0.379277	KIN
L00352	0.013622	0.009369	0.004231	0.554465	LDLR
X54304	0.013622	0.009369	0.000863	-0.19567	MLCB

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AF047487	0.013622	0.009369	0.001312	-0.33746	NCK2
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AF000152	0.013622	0.009369	0.025216	-0.34592	OS4
U02882	0.013622	0.009369	0.017536	0.892321	PDE4D
X89416	0.013622	0.009369	0.005129	-0.1405	PPP5C
U27516	0.013622	0.009369	0.004164	-0.17553	RAD52
D23660	0.013622	0.009369	0.01215	0.149327	RPL4
AB016247	0.013622	0.009369	0.019879	0.416634	SC5DL
U44754	0.013622	0.009369	0.005273	0.158396	SNAPC1
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J02973	0.013622	0.009369	0.006825	0.835338	THBD
L41690	0.013622	0.009369	0.020209	-0.32814	TRADD
X89066	0.013622	0.009369	0.000396	-0.2226	TRPC1
AB024327	0.013622	0.009369	0.031	0.260875	UNRIP
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AL080123	0.013622	0.009369	0.018447	0.215445	ZNF23
AB007885	0.013622	0.009369	0.025803	-0.22701	ZNF262
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HG3477-HT3670	0.013622	0.009369	0.00042	-0.2367	
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AA975427	0.013622	0.009369	0.002377	-0.26992	
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AL022398	0.013622	0.009369	0.017529	-0.48579	
HG2689-HT2785	0.013622	0.009369	0.029818	0.202486	
AF034373	0.013622	0.014679	0.00591	-0.26511	A2LP
X83467	0.013622	0.014679	0.006111	-0.25837	ABCD3
U41766	0.047678	0.014679	0.014363	0.473526	ADAM9
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U84011	0.013622	0.014679	0.012995	-0.2499	AGL
M74088	0.013622	0.014679	0.038601	-0.16952	APC
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U72649	0.047678	0.014679	0.029157	0.227444	BTG2
X95592	0.047678	0.014679	0.014127	0.201273	C1D
D78586	0.047678	0.014679	0.028845	-0.05709	CAD
D30742	0.047678	0.014679	0.028215	0.180381	CAMK4
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X83378	0.013622	0.014679	0.025603	0.133485	CLCN6
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S80864	0.013622	0.014679	0.011106	-0.33164	CYCL
D17530	0.047678	0.014679	0.005519	-0.15234	DBN1
U87947	0.047678	0.014679	0.011279	0.222382	EMP3
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AB028973	0.013622	0.014679	0.046458	-0.12088	FLJ10883
AL080172	0.047678	0.014679	0.02693	-0.063	FLJ21919
AF032886	0.047678	0.014679	0.009814	0.232307	FOXO3A
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M16937	0.013622	0.014679	0.002262	-0.13536	HOXB7
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X87949	0.047678	0.014679	0.028569	0.296273	HSPA5
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AL049470	0.013622	0.014679	0.010492	0.283688	HYPB
Y10659	0.047678	0.014679	0.024205	-0.1217	IL13RA1
X52015	0.047678	0.014679	0.006637	0.417081	IL1RN
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U96919	0.013622	0.014679	0.003221	-0.19947	INPP4A
U12897	0.013622	0.014679	0.002496	-0.15016	IPW
S62539	0.013622	0.014679	0.012982	-0.20615	IRS1
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W25934	0.047678	0.014679	0.016925	0.363279	JTV1
X56681	0.047678	0.014679	0.004935	0.713663	JUND
M64934	0.047678	0.014679	0.003162	-0.1823	KEL
D86975	0.047678	0.014679	0.048475	0.163408	KIAA0222
AB020701	0.013622	0.014679	0.013946	0.283086	KIAA0894
AB023141	0.047678	0.014679	0.017326	-0.33543	KIAA0924
AB023148	0.013622	0.014679	0.016218	-0.27496	KIAA0931
AB023227	0.047678	0.014679	0.043542	0.316063	KIAA1010
AB028963	0.047678	0.014679	0.039194	-0.12296	KIAA1040
AL080188	0.047678	0.014679	0.016745	-0.10387	KIAA1775
AJ224162	0.013622	0.014679	0.002225	-0.24337	LAS
L25931	0.013622	0.014679	0.00482	-0.2367	LBR
AC004410	0.047678	0.014679	0.017457	0.210096	LOC56928
AB009462	0.047678	0.014679	0.012892	0.131673	LRP3
AF077820	0.013622	0.014679	0.003095	-0.40005	LRP5
X59408	0.047678	0.014679	0.018321	-0.3029	MCP
L13773	0.013622	0.014679	0.002741	-0.18297	MLLT2
X82209	0.047678	0.014679	0.010828	0.178564	MN1
X96401	0.013622	0.014679	0.001643	0.317165	MNT
M30818	0.047678	0.014679	0.032832	0.292682	MX2

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D50692	0.013622	0.014679	0.043374	-0.20783	MYCBP
AB007191	0.013622	0.014679	0.022026	-0.18098	MYCBP
X17576	0.013622	0.014679	0.001641	-0.26027	NCK1
X61498	0.013622	0.014679	0.006234	0.307667	NFKB2
AF052093	0.047678	0.014679	0.001318	-0.31976	NJMU-R1
X00737	0.047678	0.014679	0.037385	0.219194	NP
U02020	0.047678	0.014679	0.014866	0.650286	PBEF
X66362	0.047678	0.014679	0.006159	0.137944	PCTK3
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D30037	0.047678	0.014679	0.001579	-0.21226	PITPNB
AB006746	0.047678	0.014679	0.0356	0.189986	PLSCR1
AF054182	0.013622	0.014679	0.002098	-0.54761	PMPCB
S87759	0.013622	0.014679	0.007522	0.39052	PPM1A
M13057	0.047678	0.014679	0.032523	-0.19317	PRH1
M64992	0.047678	0.014679	0.047326	0.178696	PSMA1
X58288	0.047678	0.014679	0.002633	0.409542	PTPRM
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U79716	0.013622	0.014679	0.003409	0.195389	RELN
U69198	0.047678	0.014679	0.048001	0.085316	RFNG
AF117829	0.047678	0.014679	0.003668	0.377251	RIPK2
AF039029	0.047678	0.014679	0.002146	-0.28622	RNUT1
AW021542	0.013622	0.014679	0.000677	-0.29232	SAP18
U64197	0.047678	0.014679	0.021124	0.220476	SCYA20
AB023136	0.013622	0.014679	0.00288	-0.10963	SEC15B
AF055006	0.013622	0.014679	0.011241	0.238955	SEC6
Z46606	0.047678	0.014679	0.005778	-0.1566	SMARCA3
L25270	0.047678	0.014679	0.002401	-0.15644	SMCX
M60618	0.013622	0.014679	0.006316	0.235838	SP100
AI739308	0.013622	0.014679	0.001861	-0.57419	SRP46
U52960	0.047678	0.014679	0.02599	0.429086	SURB7
D50863	0.013622	0.014679	0.006582	-0.13005	TESK1
D64015	0.013622	0.014679	0.007587	-0.3629	TIAL1
AB001523	0.047678	0.014679	0.027565	0.164838	TMEM1
L21715	0.013622	0.014679	0.000862	0.309808	TNNI2
AF045583	0.047678	0.014679	0.043887	-0.16757	TULP3
AJ001340	0.013622	0.014679	0.002396	-0.17031	U3-55K
AB015344	0.013622	0.014679	0.008107	-0.31161	UBQLN2
J03824	0.013622	0.014679	0.005864	-0.18849	UROS
AF022789	0.047678	0.014679	0.006582	0.309267	USP12
U48801	0.013622	0.014679	0.003849	-0.17743	VEGFB
HG544-HT544	0.047678	0.014679	0.010549	0.454218	
S66666	0.013622	0.014679	0.003364	-0.14303	
AI687419	0.047678	0.014679	0.039394	-0.3657	
W28800	0.047678	0.014679	0.004582	0.270831	
AL080111	0.013622	0.014679	0.001378	-0.36029	
AF070536	0.047678	0.014679	0.006685	0.199364	

AF070633	0.047678	0.014679	0.010142	-0.1635	
AF054998	0.013622	0.014679	0.007913	-0.21157	
HG3725-HT3981	0.047678	0.014679	0.027792	-0.11953	
HG1614-HT1614	0.013622	0.014679	0.006999	-0.45233	
M22324	0.013622	0.01669	0.009982	0.283293	ANPEP
AC005955	0.013622	0.01669	0.004346	0.137324	CEACAM4
S68134	0.013622	0.01669	0.005372	1.92718	CREM
S68271	0.013622	0.01669	0.009154	1.49785	CREM
M24069	0.013622	0.01669	0.003022	0.249971	CSDA
AF000984	0.013622	0.01669	0.004295	0.46432	DBY
AF055917	0.013622	0.01669	0.015434	0.102855	F2RL3
U27333	0.013622	0.01669	0.012662	0.136047	FUT6
X89887	0.013622	0.01669	0.009728	0.152829	HIRA
L42243	0.013622	0.01669	0.002638	0.218644	IFNAR2
AI950382	0.013622	0.01669	0.00744	0.601631	KIAA0585
AI950382	0.013622	0.01669	0.002126	0.519735	KIAA0585
U17760	0.013622	0.01669	0.044392	0.431131	LAMB3
L48692	0.013622	0.01669	0.041233	0.63409	LOC56902
X94232	0.013622	0.01669	0.016402	0.326694	MAPRE2
AA037278	0.013622	0.01669	0.01607	0.119411	MGC10882
L13740	0.013622	0.01669	0.007795	0.355688	NR4A1
U12767	0.013622	0.01669	0.011648	1.30268	NR4A3
D78579	0.013622	0.01669	0.005896	1.11766	NR4A3
X17042	0.013622	0.01669	0.015594	0.239796	PRG1
U48296	0.013622	0.01669	0.003124	0.864101	PTP4A1
M83221	0.013622	0.01669	0.012321	0.192956	RELB
AF107463	0.013622	0.01669	0.009662	0.419254	SPF30
L47276	0.013622	0.01669	0.004673	0.194449	TOP2A
X00734	0.013622	0.01669	0.010039	0.347307	TUBB5
X51521	0.013622	0.01669	0.010303	0.60161	VIL2
S54641	0.013622	0.01669	0.008483	0.183207	ZNF124
M91029	0.013622	0.022759	0.010686	0.450612	AMPD2
AB021638	0.136189	0.022759	0.024881	-0.1126	APBA3
AL120559	0.013622	0.022759	0.004505	0.577915	ARPP-19
AF039656	0.013622	0.022759	0.006991	0.68481	BASP1
AB020623	0.047678	0.022759	0.009696	0.418826	BCAS2
X60201	0.013622	0.022759	0.011758	-0.1576	BDNF
U56637	0.047678	0.022759	0.008899	-0.28102	CAPZA1
AW043690	0.047678	0.022759	0.031971	0.134862	CCK
D13627	0.047678	0.022759	0.019298	0.203913	CCT8
U56998	0.013622	0.022759	0.024403	0.442545	CNK
U71267	0.047678	0.022759	0.007233	-0.13426	CNOT4
F27891	0.047678	0.022759	0.02847	0.119514	COX6A2
U78524	0.013622	0.022759	0.002554	0.353034	DDXBP1
AF043733	0.047678	0.022759	0.005645	0.22771	DEDD
X64229	0.013622	0.022759	0.013033	-0.20244	DEK
AL050284	0.047678	0.022759	0.002819	0.232244	DKFZP586M1019
L05147	0.013622	0.022759	0.021168	0.111752	DUSP3
U15642	0.013622	0.022759	0.013339	0.474421	E2F5

U31556	0.047678	0.022759	0.011303	0.335871	E2F5
AC004262	0.047678	0.022759	0.004968	-0.25642	EMR2
AA181196	0.047678	0.022759	0.009459	-0.10534	FLJ11712
U74612	0.013622	0.022759	0.014802	-0.18783	FOXM1
W28281	0.013622	0.022759	0.011042	0.813742	GABARAPL1
AI183417	0.013622	0.022759	0.011016	0.117979	GABPB1
L13720	0.013622	0.022759	0.014471	-0.1601	GAS6
X15722	0.013622	0.022759	0.029451	-0.19175	GSR
Y07595	0.013622	0.022759	0.003113	-0.20996	GTF2H4
L43821	0.047678	0.022759	0.005863	-0.20401	HEF1
L10379	0.013622	0.022759	0.02006	-0.15961	HRIHFB2206
X99209	0.013622	0.022759	0.021333	-0.14942	HRMT1L1
X77956	0.013622	0.022759	0.009598	0.591031	ID1
AL021707	0.013622	0.022759	0.004161	1.79061	KIAA0063
AB007896	0.013622	0.022759	0.006273	-0.41247	KIAA0436
AB014528	0.047678	0.022759	0.001992	-0.31837	KIAA0628
AB014607	0.013622	0.022759	0.000764	-0.15753	KIAA0707
AB018290	0.013622	0.022759	0.034506	-0.28703	KIAA0747
AB018337	0.013622	0.022759	0.008466	-0.41118	KIAA0794
AB023161	0.013622	0.022759	0.018461	-0.15095	KIAA0944
AB023202	0.013622	0.022759	0.005879	-0.19156	KIAA0985
U80743	0.013622	0.022759	0.000544	-0.30322	KIAA1498
X13794	0.047678	0.022759	0.018671	-0.12764	LDHB
Z34975	0.013622	0.022759	0.012256	-0.29089	LDLC
AI341656	0.047678	0.022759	0.021482	-0.26002	LIM
X87342	0.013622	0.022759	0.006652	-0.23382	LLGL2
U29671	0.047678	0.022759	0.001133	-0.2617	MAP3K1
Z14138	0.013622	0.022759	0.00408	0.81232	MAP3K8
AI743606	0.013622	0.022759	0.00269	-0.19764	MEL
AF052183	0.013622	0.022759	0.002151	-0.19631	MGC2722
AL050356	0.013622	0.022759	0.002743	-0.42417	MINPP1
AF041081	0.013622	0.022759	0.019282	-0.21627	MN7
U59302	0.013622	0.022759	0.003859	0.280175	NCOA1
W28360	0.013622	0.022759	0.016633	0.272057	NCUBE1
U97198	0.013622	0.022759	0.001352	-0.20163	NLP_1
AA194159	0.013622	0.022759	0.004614	-0.40044	PEX10
U38964	0.013622	0.022759	0.004912	-0.23793	PMS2L8
D38498	0.013622	0.022759	0.003965	-0.58306	PMS2L9
AA996066	0.013622	0.022759	0.003514	-0.21994	PMS2L9
AB029028	0.013622	0.022759	0.027753	-0.29778	RAP140
AA402524	0.047678	0.022759	0.005359	-0.11564	RBM9
U79745	0.013622	0.022759	0.00409	0.777629	SLC16A6
X98332	0.013622	0.022759	0.002282	-0.20078	SLC22A1
D42045	0.013622	0.022759	0.006867	-0.19726	SNM1
M76231	0.013622	0.022759	0.009942	0.13899	SPR
U76366	0.013622	0.022759	0.015416	-0.09378	TCOF1
U09087	0.013622	0.022759	0.00607	-0.26017	TMPO
AF049140	0.047678	0.022759	0.011115	-0.21894	UBE2V2
AF038962	0.047678	0.022759	0.007219	-0.44337	VDAC3
D84145	0.013622	0.022759	0.002923	0.574155	WS-3

Y09723	0.047678	0.022759	0.001292	0.234149	ZNF151
AL049991	0.013622	0.022759	0.007094	0.245237	
AL050148	0.013622	0.022759	0.013128	-0.26398	
AI014538	0.013622	0.022759	0.003507	-0.15278	
AI732885	0.047678	0.022759	0.043886	-0.10293	
U14573	0.013622	0.022759	0.04259	-0.11614	
U82987	0.013622	0.024606	0.00343	-0.17272	BBC3
L12168	0.013622	0.024606	0.007944	-0.22028	CAP
V00571	0.013622	0.024606	0.005873	0.132015	CRH
AL022398	0.013622	0.024606	0.015005	-0.44535	DJ434O14.3
AL080081	0.013622	0.024606	0.007659	0.548836	DNAJB9
X85116	0.013622	0.024606	0.039531	-0.24601	EPB72
AJ007669	0.013622	0.024606	0.019404	-0.23162	FANCG
AW024285	0.013622	0.024606	0.007049	0.311562	FLJ12443
W27666	0.013622	0.024606	0.009544	-0.25685	FLJ14393
AA908993	0.013622	0.024606	0.015356	-0.12684	FLJ14393
U90917	0.013622	0.024606	0.016602	-0.23386	FOXM1
AF017445	0.013622	0.024606	0.025525	-0.33517	FPGT
AJ238764	0.013622	0.024606	0.030667	0.197763	GNE
J04501	0.013622	0.024606	0.007821	-0.23523	GYS1
X56841	0.013622	0.024606	0.022605	-0.23469	HLA-E
M63438	0.013622	0.024606	0.005389	-0.75873	IGKC
S66213	0.013622	0.024606	0.011362	-0.09802	ITGA6
AB007870	0.013622	0.024606	0.002855	0.657213	KIAA0410
N29665	0.013622	0.024606	0.008301	-0.49779	KIAA0618
AB018353	0.013622	0.024606	0.033864	-0.3542	KIAA0810
D10522	0.013622	0.024606	0.028464	0.22227	MACS
AF004709	0.013622	0.024606	0.018118	-0.09931	MAPK13
W28275	0.013622	0.024606	0.005871	-0.27591	MGC11061
AF087020	0.013622	0.024606	0.032064	-0.13544	MPZL1
U61981	0.013622	0.024606	0.012069	-0.20932	MSH3
U90942	0.013622	0.024606	0.004002	0.179029	MYO5A
D50370	0.013622	0.024606	0.008327	-0.11492	NAP1L3
U91512	0.013622	0.024606	0.00493	0.549889	NINJ1
AF069987	0.013622	0.024606	0.007336	-0.16953	NIT1
U37689	0.013622	0.024606	0.007097	-0.17369	POLR2H
L19067	0.013622	0.024606	0.006406	0.148517	RELA
X13482	0.013622	0.024606	0.016873	0.241998	SNRPA1
D16827	0.013622	0.024606	0.004314	-0.16954	SSTR5
AB011420	0.013622	0.024606	0.030791	0.171669	STK17A
L39060	0.013622	0.024606	0.026797	-0.24028	TAF1A
AB011169	0.013622	0.024606	0.004017	-0.24355	TEB4
U69108	0.013622	0.024606	0.024472	-0.17595	TRAF5
AB011004	0.013622	0.024606	0.00265	1.03158	UAP1
AB014584	0.013622	0.024606	0.028525	-0.1337	UBE4B
HG3914-HT4184	0.013622	0.024606	0.025854	-0.12454	
Z32860	0.013622	0.024606	0.002037	-0.11041	
U25849	0.013622	0.024606	0.00632	-0.43498	
AF052100	0.013622	0.024606	0.006718	-0.2297	
X59268	0.013622	0.024606	0.003586	0.479423	GTF2B

AF007142	0.013622	0.024606	0.01864	-0.34584	
AI312646	0.013622	0.024606	0.027596	-0.14991	
AL022318	0.047678	0.028192	0.049355	-0.11704	APOBEC1L
M30704	0.047678	0.028192	0.00926	0.279668	AREG
AF001307	0.047678	0.028192	0.018109	-0.12594	ARNT
AB020680	0.047678	0.028192	0.007009	0.227256	BAG5
AF018631	0.047678	0.028192	0.008344	-0.13689	BTD
D64110	0.047678	0.028192	0.022809	0.398412	BTG3
Z11697	0.047678	0.028192	0.024131	0.750492	CD83
M31516	0.047678	0.028192	0.021562	0.517068	DAF
AF000982	0.047678	0.028192	0.025357	0.29808	DDX3
L77566	0.047678	0.028192	0.01243	0.178957	DGSI
AL096725	0.047678	0.028192	0.007381	0.436688	DKFZP434B103
AL080201	0.047678	0.028192	0.044829	-0.11576	DKFZP434F162
AL050286	0.047678	0.028192	0.004267	-0.22397	DKFZP586A011
Y13350	0.047678	0.028192	0.015562	0.137002	DNAJA2
AJ223333	0.047678	0.028192	0.013836	-0.17437	DNMT2
L34075	0.047678	0.028192	0.013848	-0.25236	FRAP1
D31766	0.047678	0.028192	0.029287	-0.09623	GNPI
Z80776	0.047678	0.028192	0.002034	0.143491	H2AFG
K03183	0.047678	0.028192	0.040298	0.163306	HUMCGBBA3
X57025	0.047678	0.028192	0.009135	0.437394	IGF1
X56681	0.047678	0.028192	0.012885	0.423181	JUND
AB007916	0.047678	0.028192	0.00772	-0.45744	KIAA0447
AI672098	0.047678	0.028192	0.014331	0.160649	KIAA0934
AB029020	0.047678	0.028192	0.035285	-0.3101	KIAA1097
W27233	0.047678	0.028192	0.019918	-0.24802	KIDINS220
AL049341	0.047678	0.028192	0.001943	-0.3086	LOC57209
AL049422	0.047678	0.028192	0.028823	0.264129	LOC84549
AF010193	0.047678	0.028192	0.003729	0.927225	MADH7
AF007134	0.047678	0.028192	0.009151	-0.1209	MAPK8IP1
L04731	0.047678	0.028192	0.025599	-0.07236	MLL
AB014547	0.047678	0.028192	0.023787	-0.15831	MTMR4
U91616	0.047678	0.028192	0.018681	0.377931	NFKBIE
X75918	0.047678	0.028192	0.019713	1.21948	NR4A2
AL049842	0.047678	0.028192	0.022698	0.201258	NUFIP1
U57843	0.047678	0.028192	0.011796	-0.13969	PIK3CD
S76965	0.047678	0.028192	0.012413	0.426208	PKIA
AL023553	0.047678	0.028192	0.00321	-0.15608	PMM1
M93425	0.047678	0.028192	0.019899	-0.36854	PTPN12
AF044968	0.047678	0.028192	0.006887	0.121898	PVRL2
M28211	0.047678	0.028192	0.050065	-0.08518	RAB4
AF083255	0.047678	0.028192	0.021248	-0.27368	RNAHP
U04897	0.047678	0.028192	0.013893	0.278167	RORA
AL031228	0.047678	0.028192	0.020491	-0.22382	SACM2L
Y08262	0.047678	0.028192	0.008184	-0.34195	SCA2
AF000652	0.047678	0.028192	0.001533	0.415218	SDCBP
D31891	0.047678	0.028192	0.00536	-0.18144	SETDB1
X66079	0.047678	0.028192	0.008707	0.129642	SPIB
Z96932	0.047678	0.028192	0.013622	-0.14003	SSNA1

D43642	0.047678	0.028192	0.015302	-0.26409	TCFL1
D50919	0.047678	0.028192	0.016207	-0.23972	TRIM14
X01703	0.047678	0.028192	0.004339	0.386096	TUBA3
AF022375	0.047678	0.028192	0.015198	0.503607	VEGF
AF062346	0.047678	0.028192	0.014763	0.455053	ZNF216
J04755	0.047678	0.028192	0.014444	0.302274	
AA524802	0.047678	0.028192	0.036226	-0.24775	
AL096749	0.047678	0.028192	0.017041	0.106309	
M21259	0.047678	0.028192	0.025927	0.18378	
X61587	0.047678	0.037364	0.024028	0.222788	ARHG
J04027	0.047678	0.037364	0.019918	0.336927	ATP2B1
W28091	0.047678	0.037364	0.016936	-0.1567	BBS4
U03106	0.047678	0.037364	0.004064	0.915096	CDKN1A
AL049924	0.047678	0.037364	0.001517	-0.23208	DKFZP547G1110
L19161	0.047678	0.037364	0.006578	-0.49859	EIF2S3
AF052123	0.136189	0.037364	0.013524	-0.24445	FLJ10814
AA522530	0.047678	0.037364	0.038021	0.413536	FLJ20500
AJ011001	0.047678	0.037364	0.016436	-0.63045	GPR56
U50079	0.047678	0.037364	0.013178	-0.37546	HDAC1
AI796944	0.047678	0.037364	0.011597	0.216392	HIS1
S82986	0.047678	0.037364	0.006441	-0.20652	HOXC6
AB011173	0.047678	0.037364	0.01376	-0.26283	KIAA0601
AB023160	0.047678	0.037364	0.029467	-0.23276	KIAA0943
AJ001685	0.047678	0.037364	0.015208	-0.48906	KLRC3
AJ000673	0.047678	0.037364	0.009021	-0.38103	KLRD1
AB002450	0.047678	0.037364	0.003391	-0.37426	LOC51014
U68385	0.047678	0.037364	0.007651	-0.16327	MEIS3
AI688516	0.047678	0.037364	0.017859	-0.15146	NDUFA2
W28770	0.047678	0.037364	0.005269	-0.16121	NP25
L41827	0.047678	0.037364	0.011308	0.139896	NRG1
X84373	0.047678	0.037364	0.00725	0.77533	NRIP1
M25897	0.047678	0.037364	0.025747	-0.41462	PF4
U50062	0.047678	0.037364	0.018154	0.19401	RIPK1
AJ011785	0.047678	0.037364	0.017907	-0.07616	SIX6
X70683	0.047678	0.037364	0.0155	-0.10219	SOX4
AL035699	0.047678	0.037364	0.006561	-0.15185	TBPL1
D15050	0.047678	0.037364	0.016133	0.990791	TCF8
AF017146	0.047678	0.037364	0.002975	-0.20652	TOP3B
U54996	0.047678	0.037364	0.00691	-0.17359	ZW10
HG4234-HT4504	0.047678	0.037364	0.003258	-0.13985	
X04500	0.047678	0.058634	0.02228	0.857952	IL1B

Table IV: Differential Gene Expression in MOG-reactive T-cells- MS vs. Healthy

Identifier	Symbol	Name	Function	Fold Change	Pvalue t-test
Up regulated M35878	IGFBP3	insulin-like growth factor binding protein 3	modulate IGF activity	5.8	0.03
AB002318	KIAA0320	KIAA0320 protein		2.4	0.05
AF024710	VEGF	vascular endothelial growth factor	endothelial cell proliferation	2.3	0.02
AA628946	KHSRP	KH-type splicing regulatory protein	mRNA processing	2.2	0.01
L42374	PPP2R5B	protein phosphatase 2, regulatory subunit B	protein phosphatase	2.1	0.05
U54644	TUB	tubby (mouse) homolog	may be a transcription factor	1.8	0.01
AB023167	KIAA0950	lifeguard	Apoptosis	1.8	0.006
X62654	CD63	CD63 antigen (melanoma 1 antigen)	growth regulation	1.8	0.03
H98552		cDNA DKFZp586I0523		1.8	0.01
AL050395	MOF	member of MYST acetyl transferases	histone acetyl transferases	1.7	0.03
L27213	SLC4A3	solute carrier family 4, anion exchange 3	inorganic anion exchanger	1.7	0.01
AF014837	M6A	putative methyltransferase	Transcription factor	1.6	0.05
AB014537	KIAA0637	KIAA0637 gene product	Apoptosis	1.5	0.003
D13969	ZNF144	zinc finger protein 144 (Mel-18)	DNA-Binding protein	1.5	0.04
AJ012590	H6PD	hexose-6-phosphate dehydrogenase	Oxidoreductase	1.5	0.04
M13995	BCL2	B-cell CLL/lymphoma 2	Apoptosis	1.5	0.03
AI760801		chromosome 19, cosmid R31180		1.5	0.009
AI660963	MAP3K12	mitogen-activated protein 3 kinase 12	Transferase cytoplasmic	1.5	0.02
Down regulated D45248	PSME2	proteasome activator subunit 2 (PA28 beta)	Protein degradation	-1.5	0.04
W28612		ESTs		-1.5	0.02
Z46389	VASP	vasodilator-stimulated phosphoprotein	Signal transduction	-1.6	0.02
AA152202	FLJ14639	hypothetical protein FLJ14639		-1.6	0.02
AF080561	RBM14	RNA binding motif protein 14	RNA binding protein	-1.7	0.03
D50922	KIAA0132	Kelch-like ECH-associated protein 1	ECH-associated protein 1	-1.7	0.03
AF025441	OIP5	Opa-interacting protein 5		-1.8	0.04
AF080227	EED	embryonic ectoderm development	transcriptional repressor	-1.8	0.04

D87957	RQCD1	required for cell differentiation	sex differentiation	-1.9	0.03
X61498	NFKB2	nuclear factor of kappa light polypeptide Bcells	expression of inflammatory genes	-1.9	0.05
X52425	IL4R	interleukin 4 receptor	receptor signalling protein	-2	0.04
L08069	DNAJA1	DnaJ (Hsp40) homolog, subfamily A, member 1	protein folding and transport	-2	0.04
AF071504	STX11	syntaxin 11	protein transport	-2.1	0.03
M11717	HSPA1A	heat shock 70kD protein 1A	heat shock response	-2.2	0.03
M59830	HSPA1B	heat shock 70kD protein 1B	heat shock response	-2.2	0.03
M16441	TNF	Human tumor necrosis factor	Inflammatory response	-2.3	0.05
D89077	SLA	Src-like-adapter		-2.4	0.05
U77949	CDC6	cell division cycle 6, S. cerevisiae homolog	DNA replication checkpoint	-2.5	0.02
D38549	KIAA0068	KIAA0068 protein		-2.5	0.01
L23959	TFDP1	transcription factor Dp-1	cycle progression G1 to S-phase	-2.5	0.01
L78833	BRCA1	Breast cancer susceptibility gene		-2.7	0.04
M63193	ECGF1	endothelial cell growth factor 1	stimulates angiogenesis	-2.8	0.01
AF035625	STK11	serine/threonine kinase 11	Peutz-Jeghers syndrome	-2.9	0.04
J04130	SCYA4	small inducible cytokine A4	Cell-to-cell signalling	-2.9	0.05
X93086	BLVRA	biliverdin reductase A	biliverdin reductase	-4	0.03

Table V: Differential Gene Expression in Probable MS vs. Healthy

Identification	TNOM PValue	Info PValue	t-Test PValue	Log Fold Change	Gene Symbol
NM_018049.1	0.000233	0.000233	2.46E-05	0.438337	FLJ10297
NM_005886.1	0.000233	0.000233	0.000553	0.35972	KATNB1
NM_000161.1	0.000233	0.000233	0.000297	-0.48848	GCH1
NM_001539.1	0.000233	0.000233	0.000144	-0.58017	DNAJA1
AF349571.1	0.004202	0.004202	0.000274	1.78925	HBA1
M25079.1	0.004202	0.004202	0.000247	1.59503	HBB
V00489	0.004202	0.004202	0.000268	1.54947	
BC005931.1	0.004202	0.004202	0.000296	1.48707	HBA2
T50399	0.004202	0.004202	0.000275	1.43533	HBA2
NM_024567.1	0.004202	0.004202	0.002206	1.42146	FLJ21616
AF105974.1	0.004202	0.004202	0.001086	1.3896	HBA1
NM_000558.2	0.004202	0.004202	0.000707	1.3348	HBA1
AI133353	0.004202	0.004202	0.000897	1.29746	HBG2
AF059180	0.004202	0.004202	0.000309	1.29355	
AF349114.1	0.004202	0.004202	0.000163	1.27511	HBB
BE547674	0.004202	0.004202	0.002947	0.636619	
NM_012452.1	0.004202	0.004202	0.000541	0.570818	TNFRSF13B

AA314406	0.004202	0.001401	0.002013	0.520631	TRAP95
NM_015909.1	0.004202	0.001401	0.000398	0.501733	NAG
NM_006868.1	0.004202	0.004202	0.002711	0.49862	RAB31
BC000305.1	0.004202	0.004202	0.006921	0.475733	CASP6
L77566	0.004202	0.001401	0.00033	0.446293	DGSI
BF971416	0.004202	0.004202	0.002405	0.410742	DKFZP586N0721
BE879367	0.004202	0.004202	0.00056	0.382484	AKAP2
NM_001640.2	0.004202	0.001401	0.004091	0.36631	APEH
BC001808.1	0.004202	0.004202	0.012997	0.347043	NM23-H6
AL049539	0.004202	0.004202	0.010738	0.2822	KIAA0255
BC000580.1	0.004202	0.001401	0.014166	0.270658	PH-4
NM_012151.2	0.004202	0.001401	0.000685	0.267664	F8A
BC004423.1	0.004202	0.004202	0.012194	0.249144	TNRC5
NM_004890.1	0.004202	0.001401	0.010332	0.134439	SPAG7
AB029040	0.004202	0.004202	0.010819	-0.14172	KIAA1117
NM_025160.1	0.004202	0.001401	0.004986	-0.21141	FLJ21016
AW162015	0.004202	0.004202	0.301224	-0.24766	ZNF143
NM_005574.2	0.004202	0.004202	0.107595	-0.24939	LMO2
NM_014670.1	0.004202	0.004202	0.025534	-0.27225	BZW1
AL117643.1	0.004202	0.004202	0.046495	-0.27766	
AA628948	0.004202	0.001401	0.000319	-0.28951	ADSS
AF251062.1	0.004202	0.001401	0.000435	-0.30924	LOC84549
AL564683	0.004202	0.004202	0.018258	-0.44633	CEBPB
NM_014999.1	0.004202	0.004202	0.001021	-0.47304	RAB21
NM_017723.1	0.004202	0.004202	0.02759	-0.49548	FLJ20245
NM_003264.1	0.004202	0.004202	0.002592	-0.49551	TLR2
AF062347.1	0.004202	0.004202	0.00529	-0.51432	ZNF216
NM_004556.1	0.004202	0.004202	0.001134	-0.53489	NFKBIE
U92014.1	0.004202	0.004202	0.003064	-0.59511	
NM_014778.1	0.004202	0.004202	0.001106	-0.65156	KIAA0410
NM_015384.1	0.004202	0.004202	0.002943	-0.68193	IDN3
AK022513.1	0.004202	0.004202	0.001326	-0.68416	DUSP10
NM_003246.1	0.004202	0.001401	0.000162	-1.44745	THBS1
AI812030	0.004202	0.001401	7.42E-05	-1.51098	THBS1
NM_000559.1	0.035714	0.035247	0.006202	1.93991	HBG1
NM_000184.1	0.035714	0.04225	0.009164	1.67513	HBG2
NM_005564.1	0.035714	0.04225	0.010814	1.03322	LCN2
AF274863.1	0.035714	0.00747	0.007719	0.952868	SEC31B-1
NM_002288.2	0.035714	0.015406	0.010689	0.834313	LAIR2
M87789.1	0.035714	0.04225	0.058518	0.79032	IGHG3
NM_005764.1	0.035714	0.04225	0.053679	0.789147	DD96
AK000168.1	0.035714	0.04225	0.038176	0.763766	KIAA1919
NM_020037.1	0.035714	0.035247	0.061379	0.746143	ABCC3
AF103529.1	0.035714	0.035247	0.015284	0.736268	
AV698647	0.035714	0.035247	0.017411	0.616137	IGLJ3
AI357539	0.035714	0.04225	0.00558	0.601843	MGC4126
NM_015935.1	0.035714	0.035247	0.021683	0.593818	CGI-01
D38535	0.035714	0.04225	0.016025	0.571168	ITIH4
AA723370	0.035714	0.04225	0.039917	0.570325	LOC51011
AF227968.1	0.035714	0.00747	0.005308	0.566516	SH2B
X12530.1	0.035714	0.04225	0.056335	0.559172	MS4A1

AI348935	0.035714	0.035247	0.014129	0.546773	CALR
NM_003422.1	0.035714	0.04225	0.006737	0.536815	ZNF42
NM_015559.1	0.035714	0.04225	0.028795	0.536316	SETBP1
NM_013378.1	0.035714	0.035247	0.005191	0.532564	VPREB3
NM_004912.1	0.035714	0.015406	0.003037	0.52082	CCM1
NM_006230.1	0.035714	0.015406	0.007471	0.517979	POLD2
NM_006235.1	0.035714	0.035247	0.021726	0.515263	POU2AF1
AL037557	0.035714	0.00747	0.002786	0.511724	POLR2I
NM_014703.1	0.035714	0.00747	0.006709	0.4938	KIAA0800
NM_015670.1	0.035714	0.035247	0.045708	0.464156	SENP3
AA643304	0.035714	0.015406	0.004712	0.459694	
AI948503	0.035714	0.04225	0.017964	0.45625	ABCC4
BC002807.1	0.035714	0.04225	0.100759	0.455683	MS4A1
AF123539.1	0.035714	0.035247	0.028286	0.454603	HTCD37
AA149644	0.035714	0.00747	0.02413	0.450082	JAM3
BC000585.1	0.035714	0.04225	0.033113	0.44368	SLC21A11
AB044806.1	0.035714	0.04225	0.007766	0.433985	KCNH2
U37025	0.035714	0.035247	0.046971	0.427213	SULT1A1
NM_020166.2	0.035714	0.035247	0.006318	0.423798	MCCC1
NM_002876.1	0.035714	0.035247	0.026644	0.414867	RAD51C
NM_002387.1	0.035714	0.035247	0.01092	0.409481	MCC
NM_005816.1	0.035714	0.04225	0.103051	0.407348	TACTILE
H95263	0.035714	0.035247	0.069113	0.406766	
NM_003146.1	0.035714	0.035247	0.003146	0.405309	SSRP1
NM_003550.1	0.035714	0.035247	0.054105	0.403851	MAD1L1
AK022494.1	0.035714	0.00747	0.001189	0.397073	RAB3GAP
NM_006400.2	0.035714	0.035247	0.021072	0.396297	DCTN2
NM_006012.1	0.035714	0.035247	0.015241	0.394779	CLPP
NM_014921.1	0.035714	0.035247	0.014463	0.394308	LEC2
NM_025056.1	0.035714	0.00747	0.01912	0.393739	FLJ23185
NM_003573.1	0.035714	0.04225	0.026053	0.393337	LTBP4
NM_000132.2	0.035714	0.035247	0.005292	0.392442	F8
AF031824.1	0.035714	0.035247	0.190243	0.389129	CST7
NM_001841.1	0.035714	0.035247	0.07115	0.387067	CNR2
NM_018391.1	0.035714	0.035247	0.138584	0.386982	FLJ23277
U79248.1	0.035714	0.00747	0.007475	0.386419	
NM_024332.1	0.035714	0.04225	0.039154	0.386198	C6.1A
BF510692	0.035714	0.04225	0.046782	0.385324	PAX5
AA243774	0.035714	0.035247	0.050456	0.381631	MMP24
AL121964	0.035714	0.035247	0.107681	0.373759	MAP3K7
L25275.1	0.035714	0.035247	0.020684	0.372971	SULT1A3
AB018289.1	0.035714	0.035247	0.002286	0.37263	KIAA0746
NM_000294.1	0.035714	0.035247	0.011432	0.367693	PHKG2
BC001906.1	0.035714	0.035247	0.107947	0.366899	MTX1
NM_000651.1	0.035714	0.04225	0.047953	0.365471	CR1
NM_001667.1	0.035714	0.00747	0.009661	0.362105	ARL2
AI133727	0.035714	0.00747	0.018354	0.358884	ZAP
BC002873.1	0.035714	0.035247	0.048711	0.358052	DKFZP564J0123
NM_004178.2	0.035714	0.035247	0.007313	0.356459	TARBP2
BG532929	0.035714	0.035247	0.037215	0.356254	SSB
NM_018094.1	0.035714	0.035247	0.014302	0.351314	GSPT2

AC004531	0.035714	0.00747	0.01714	0.350445	DDX28
NM_001981.1	0.035714	0.035247	0.010776	0.347051	EPS15
AB020689.1	0.035714	0.035247	0.024594	0.346253	KIAA0882
NM_001055.1	0.035714	0.035247	0.056416	0.344937	SULT1A1
NM_022067.1	0.035714	0.035247	0.001332	0.337713	FLJ12707
NM_000195.1	0.035714	0.00747	0.014156	0.3312	HPS1
NM_022914.1	0.035714	0.00747	0.167735	0.331082	24432
NM_003627.1	0.035714	0.035247	0.062759	0.330371	POV1
NM_022060.1	0.035714	0.035247	0.010717	0.328122	FLJ12816
BF446180	0.035714	0.035247	0.02537	0.326347	PDCD2
U28169.1	0.035714	0.035247	0.0891	0.326218	SULT1A2
AF316873.1	0.035714	0.035247	0.022727	0.3257	PINK1
NM_017615.1	0.035714	0.035247	0.087717	0.325056	FLJ20003
NM_015853.1	0.035714	0.035247	0.021537	0.321089	LOC51035
NM_018449.1	0.035714	0.035247	0.01461	0.318475	UBAP2
NM_007056.1	0.035714	0.035247	0.013827	0.318086	SWAP2
AV702994	0.035714	0.035247	0.010766	0.316138	LOC51668
AK021884.1	0.035714	0.04225	0.016862	0.315879	NPEPPS
U64898.1	0.035714	0.035247	0.012705	0.309446	NRD1
AI431902	0.035714	0.035247	0.026163	0.307321	FLJ13491
NM_003689.1	0.035714	0.04225	0.03366	0.306281	AKR7A2
BE791629	0.035714	0.00747	0.039522	0.304821	CGTHBA
NM_016194.1	0.035714	0.035247	0.060249	0.303474	GNB5
NM_014965.1	0.035714	0.035247	0.013547	0.298042	KIAA1042
NM_003363.1	0.035714	0.035247	0.018393	0.295239	USP4
U88964	0.035714	0.035247	0.019349	0.294427	ISG20
BC001782.1	0.035714	0.035247	0.059026	0.293156	GAS2L1
BC004361.1	0.035714	0.04225	0.084538	0.292509	PSCD2
NM_017840.1	0.035714	0.035247	0.003929	0.290472	MRPL16
NM_006321.1	0.035714	0.015406	0.006688	0.288723	ARIH2
AI341234	0.035714	0.035247	0.007356	0.284699	CORO1B
N20923	0.035714	0.035247	0.020271	0.280552	FYN
L42531.1	0.035714	0.035247	0.008554	0.280023	
AK000818.1	0.035714	0.035247	0.02226	0.277695	FLJ20811
NM_000633.1	0.035714	0.035247	0.044639	0.276897	BCL2
BE551347	0.035714	0.035247	0.209003	0.276406	FLJ13052
AK000161.1	0.035714	0.04225	0.016752	0.276103	FLJ20154
AI798908	0.035714	0.04225	0.015969	0.274921	KIAA0226
NM_005111.1	0.035714	0.035247	0.01405	0.273732	CRYZL1
NM_024551.1	0.035714	0.035247	0.00372	0.272684	FLJ21432
BC006214.1	0.035714	0.00747	0.006244	0.268704	IRO039700
AI123527	0.035714	0.04225	0.105392	0.268349	KIAA0092
NM_004379.1	0.035714	0.035247	0.047229	0.267796	CREB1
AA643304	0.035714	0.035247	0.039678	0.258201	
NM_013417.1	0.035714	0.035247	0.047087	0.257738	IARS
AK025432.1	0.035714	0.035247	0.051871	0.257456	KIAA0564
AB028960	0.035714	0.04225	0.040942	0.254827	KIAA1037
NM_000048.1	0.035714	0.04225	0.038931	0.254447	ASL
NM_002808.1	0.035714	0.035247	0.023966	0.250129	PSMD2
NM_001054.1	0.035714	0.035247	0.062598	0.248696	SULT1A2
NM_005428.2	0.035714	0.035247	0.007185	0.248439	VAV1

NM_022758.1	0.035714	0.04225	0.011489	0.246401	FLJ22195
AY009128.1	0.035714	0.035247	0.084938	0.246257	NIFU
AB017004.1	0.035714	0.035247	0.079567	0.244954	PMS2L8
NM_000249.1	0.035714	0.04225	0.021274	0.243441	MLH1
U51007.1	0.035714	0.035247	0.042753	0.242223	
BC002640.1	0.035714	0.035247	0.074751	0.240603	
NM_016284.1	0.035714	0.00747	0.001929	0.240076	KIAA1007
NM_002414.1	0.035714	0.035247	0.063998	0.239013	MIC2
BC000212.1	0.035714	0.035247	0.021052	0.237577	GTF3C2
NM_004398.2	0.035714	0.035247	0.040656	0.235252	DDX10
NM_024713.1	0.035714	0.035247	0.048887	0.234927	FLJ22557
NM_002810.1	0.035714	0.035247	0.038558	0.234593	PSMD4
NM_030580.1	0.035714	0.035247	0.031263	0.233466	MGC10520
AB007896.1	0.035714	0.035247	0.211816	0.231563	KIAA0436
NM_003954.1	0.035714	0.04225	0.051916	0.230862	MAP3K14
NM_025207.1	0.035714	0.035247	0.020823	0.230015	PP591
NM_016323.1	0.035714	0.035247	0.051393	0.228764	LOC51191
NM_016069.1	0.035714	0.04225	0.132766	0.223618	Magmas
NM_013349.1	0.035714	0.035247	0.028748	0.223073	SPUF
NM_000884.1	0.035714	0.035247	0.064347	0.222421	IMPDH2
BG167570	0.035714	0.04225	0.108243	0.219652	DKFZp762N1910
NM_004551.1	0.035714	0.00747	0.06025	0.217427	NDUFS3
BG231932	0.035714	0.04225	0.079649	0.210447	CLN2
NM_017851.1	0.035714	0.035247	0.036308	0.209956	FLJ20509
NM_006519.1	0.035714	0.035247	0.032991	0.202387	TCTEL1
AF032900.1	0.035714	0.035247	0.174549	0.200739	COQ7
AL535380	0.035714	0.035247	0.265205	0.198073	BTG1
AW118862	0.035714	0.035247	0.02173	0.193753	RREB1
NM_000382.1	0.035714	0.035247	0.27948	0.193509	ALDH3A2
NM_024419.1	0.035714	0.035247	0.164883	0.190623	PGS1
NM_003904.1	0.035714	0.035247	0.245676	0.190422	ZNF259
AI928526	0.035714	0.00747	0.036861	0.185624	JTV1
NM_024581.1	0.035714	0.035247	0.230867	0.185323	FLJ13942
AF085357.1	0.035714	0.035247	0.110175	0.184965	FLOT1
NM_004475.1	0.035714	0.035247	0.072642	0.180483	FLOT2
AF334103.1	0.035714	0.00747	0.009664	0.17511	GU2
NM_017829.1	0.035714	0.035247	0.110207	0.174515	CECR5
NM_004214.3	0.035714	0.04225	0.016835	0.157902	FIBP
NM_017704.1	0.035714	0.04225	0.16159	0.157672	FLJ20189
NM_003592.1	0.035714	0.035247	0.038652	0.146241	CUL1
AI537887	0.035714	0.035247	0.467375	0.139355	EPB72
NM_023935.1	0.035714	0.035247	0.049119	0.125305	C20orf116
BG398414	0.035714	0.035247	0.286856	0.123085	RPA1
NM_016243.1	0.035714	0.035247	0.279995	0.121894	LOC51706
NM_012199.1	0.035714	0.035247	0.093241	0.118547	EIF2C1
AK024029.1	0.035714	0.04225	0.450393	0.11646	MAP-1
NM_004848.1	0.035714	0.035247	0.486492	0.113516	ICB-1
AF144638.1	0.035714	0.035247	0.255571	0.10089	SGPL1
D86062.1	0.035714	0.035247	0.532398	0.084417	C21orf33
NM_000655.2	0.035714	0.035247	0.535745	0.081167	SELL
NM_018643.1	0.035714	0.035247	0.870775	0.057399	TREM1

NM_018326.1	0.035714	0.035247	0.929375	0.035048	HIMAP4
NM_005371.2	0.035714	0.035247	0.876737	0.025127	METTL1
NM_007002.1	0.035714	0.035247	0.911541	0.010422	ADRM1
NM_004723.1	0.035714	0.035247	0.975685	-0.00562	ARHGEF2
U31501	0.035714	0.035247	0.724549	-0.0658	FXR2
NM_005338.3	0.035714	0.04225	0.126911	-0.0661	HIP1
AB006589.1	0.035714	0.035247	0.00542	-0.10655	ESR2
AA868754	0.035714	0.035247	0.304519	-0.10746	KIAA0650
AU144792	0.035714	0.035247	0.008623	-0.11362	
AF320999.1	0.035714	0.035247	0.289096	-0.11449	RTN4
NM_013229.1	0.035714	0.035247	0.529181	-0.13735	APAF1
NM_018690.1	0.035714	0.04225	0.261146	-0.14482	APOB48R
D42055.1	0.035714	0.04225	0.007978	-0.14841	NEDD4
BF968633	0.035714	0.035247	0.135003	-0.14873	RNF4
AK026678.1	0.035714	0.035247	0.00833	-0.15056	STAG2
NM_014671.1	0.035714	0.035247	0.392979	-0.15386	KIAA0010
NM_030979.1	0.035714	0.035247	0.087494	-0.15652	PABPC3
BG429214	0.035714	0.035247	0.273519	-0.15766	
NM_006892.1	0.035714	0.035247	0.001922	-0.15828	DNMT3B
NM_018975.1	0.035714	0.035247	0.042202	-0.16723	RAP1
AL137335.1	0.035714	0.035247	0.306422	-0.17292	RANBP7
NM_014016.1	0.035714	0.035247	0.398036	-0.17365	SACM1L
NM_012198.1	0.035714	0.035247	0.391555	-0.17556	GCA
NM_024586.1	0.035714	0.04225	0.011965	-0.19298	OSBPL9
N64643	0.035714	0.035247	0.16498	-0.19313	KIAA0625
NM_005951.1	0.035714	0.035247	0.156965	-0.1942	MT1H
NM_002264.1	0.035714	0.035247	0.138195	-0.1949	
AF182415.1	0.035714	0.04225	0.325959	-0.19495	RBM8A
BE674061	0.035714	0.035247	0.015036	-0.20133	PIN4
NM_004973.2	0.035714	0.00747	0.103071	-0.20162	JMJ
U58852.1	0.035714	0.035247	0.510508	-0.20606	NPAT
NM_005565.2	0.035714	0.035247	0.037541	-0.2105	LCP2
NM_004941.1	0.035714	0.035247	0.229189	-0.21215	DDX8
U02297.1	0.035714	0.035247	0.252672	-0.21782	SELPLG
NM_002940.1	0.035714	0.035247	0.112373	-0.22731	ABCE1
AL550657	0.035714	0.035247	0.069403	-0.23303	BSG
BG387770	0.035714	0.035247	0.032984	-0.2362	MGC32104
AL050205.1	0.035714	0.04225	0.352078	-0.23748	LOC113251
NM_016653.1	0.035714	0.035247	0.003387	-0.23765	ZAK
AA742237	0.035714	0.035247	0.120935	-0.23853	BAT2
NM_021183.1	0.035714	0.035247	0.069121	-0.24239	LOC57826
AB014527.1	0.035714	0.035247	0.005636	-0.24315	CLASP2
AF091086.1	0.035714	0.035247	0.124853	-0.24621	CL640
NM_006748.1	0.035714	0.04225	0.141473	-0.24728	SLA
NM_025238.1	0.035714	0.035247	0.046507	-0.24841	BTBD1
NM_018638.2	0.035714	0.035247	0.074405	-0.24942	EKI1
NM_002913.1	0.035714	0.04225	0.092197	-0.24967	
NM_002863.1	0.035714	0.035247	0.034567	-0.25494	PYGL
AF226044.1	0.035714	0.035247	0.023966	-0.25679	SNRK
NM_016217.1	0.035714	0.035247	0.01673	-0.25733	LOC51696
AF084943.1	0.035714	0.035247	0.024841	-0.26011	MINPP1

N22548	0.035714	0.04225	0.03686	-0.26164	ROCK1
AF033850.1	0.035714	0.035247	0.110532	-0.26338	PLD2
NM_014445.1	0.035714	0.00747	0.007058	-0.26858	SERP1
NM_016196.1	0.035714	0.035247	0.014278	-0.27109	KIAA0682
NM_012252.1	0.035714	0.035247	0.020625	-0.27124	TFEC
W72082	0.035714	0.035247	0.180599	-0.27284	C1QR1
NM_016166.1	0.035714	0.035247	0.071782	-0.27429	PIAS1
NM_022470.1	0.035714	0.035247	0.072884	-0.27655	WIG1
NM_030797.1	0.035714	0.035247	0.039197	-0.27728	DKFZP566A1524
NM_002199.2	0.035714	0.035247	0.250656	-0.27789	IRF2
BC003360.1	0.035714	0.035247	0.02171	-0.27851	DDX18
NM_004504.2	0.035714	0.035247	0.020834	-0.27873	HRB
NM_012072.2	0.035714	0.035247	0.118494	-0.27892	C1QR1
NM_018230.1	0.035714	0.035247	0.071301	-0.28019	NUP133
NM_002727.1	0.035714	0.04225	0.038559	-0.28438	PRG1
BC005338.1	0.035714	0.035247	0.114062	-0.28524	CAPZA2
U60521.1	0.035714	0.04225	0.066643	-0.29174	CASP9
AW188198	0.035714	0.035247	0.005126	-0.29178	TNFAIP6
BE908931	0.035714	0.035247	0.017009	-0.29572	
U64661	0.035714	0.04225	0.030982	-0.29704	
AL021395	0.035714	0.04225	0.02084	-0.29857	
NM_015176.1	0.035714	0.035247	0.059688	-0.299	KIAA0483
NM_002857.1	0.035714	0.04225	0.04761	-0.29944	PXF
U70451.1	0.035714	0.035247	0.003458	-0.30169	MYD88
NM_018042.1	0.035714	0.035247	0.020209	-0.30409	FLJ10260
AL049265.1	0.035714	0.04225	0.136618	-0.30472	
NM_024081.1	0.035714	0.035247	0.020267	-0.30513	TMG4
AI796169	0.035714	0.035247	0.023959	-0.31104	GATA3
AA160522	0.035714	0.035247	0.056044	-0.31114	UBE3A
AL136621.1	0.035714	0.04225	0.06859	-0.31538	ZNF198
NM_003051.1	0.035714	0.035247	0.028776	-0.3171	SLC16A1
AW572909	0.035714	0.035247	0.027025	-0.31713	KIAA0874
NM_017782.1	0.035714	0.04225	0.017104	-0.32078	FLJ20360
AK001821.1	0.035714	0.04225	0.013182	-0.32145	MGC4170
AW001847	0.035714	0.035247	0.204195	-0.32259	APLP2
BF196931	0.035714	0.04225	0.003706	-0.3226	ZFP95
AJ223333.1	0.035714	0.035247	0.023593	-0.32279	DNMT2
NM_005213.1	0.035714	0.04225	0.216305	-0.32285	CSTA
AF142419.1	0.035714	0.04225	0.013772	-0.33425	QKI
NM_020375.1	0.035714	0.035247	0.07666	-0.33473	C12orf5
NM_021970.1	0.035714	0.04225	0.054987	-0.33505	MAP2K1IP1
AK023816.1	0.035714	0.035247	0.136952	-0.34214	
NM_012238.3	0.035714	0.00747	0.018308	-0.3438	SIRT1
AF205218.1	0.035714	0.035247	0.033088	-0.34674	NS1-BP
NM_001660.2	0.035714	0.035247	0.020387	-0.35015	ARF4
NM_001196.1	0.035714	0.015406	0.020544	-0.35511	BID
NM_002970.1	0.035714	0.035247	0.064201	-0.35676	SAT
AC074331	0.035714	0.035247	0.01515	-0.35767	
M75715.1	0.035714	0.035247	0.010802	-0.3577	ETF1
NM_018657.2	0.035714	0.04225	0.021807	-0.3681	MYNN
NM_003370.1	0.035714	0.035247	0.056143	-0.37617	VASP

AI761561	0.035714	0.035247	0.084393	-0.37861	HK2
NM_002657.2	0.035714	0.035247	0.043402	-0.39004	PLAGL2
NM_004565.1	0.035714	0.035247	0.086212	-0.39025	PEX14
AK023837.1	0.035714	0.04225	0.083366	-0.39056	KIAA1025
AL117354	0.035714	0.00747	0.011916	-0.39754	LOC50999
NM_001356.2	0.035714	0.035247	0.029134	-0.41337	DDX3
NM_018573.1	0.035714	0.015406	0.00529	-0.41757	PRO1068
NM_030799.1	0.035714	0.035247	0.075235	-0.42088	SMAP-5
AA524053	0.035714	0.04225	0.031361	-0.42442	
NM_002748.1	0.035714	0.035247	0.023266	-0.42563	MAPK6
NM_002053.1	0.035714	0.035247	0.053201	-0.43747	GBP1
AB023227.1	0.035714	0.04225	0.003343	-0.43985	KIAA1010
AW193511	0.035714	0.035247	0.012709	-0.44652	HIS1
AW272611	0.035714	0.04225	0.024277	-0.44899	TMPO
AI671747	0.035714	0.00747	0.02288	-0.45263	MISS
AI688580	0.035714	0.035247	0.035918	-0.45484	SURB7
NM_002502.1	0.035714	0.035247	0.107712	-0.45745	NFKB2
NM_004267.1	0.035714	0.04225	0.030352	-0.47177	CHST2
X15132.1	0.035714	0.035247	0.041452	-0.47259	SOD2
NM_012093.1	0.035714	0.035247	0.011606	-0.47474	AK5
D26067.1	0.035714	0.035247	0.003438	-0.47644	KIAA0033
NM_001166.2	0.035714	0.04225	0.015252	-0.48334	BIRC2
NM_016545.1	0.035714	0.035247	0.029826	-0.48723	IER5
NM_021122.2	0.035714	0.035247	0.070882	-0.49855	FACL2
NM_017936.1	0.035714	0.035247	0.008293	-0.5016	FLJ20707
NM_000574.1	0.035714	0.035247	0.022743	-0.50532	DAF
AL050144.1	0.035714	0.015406	0.000822	-0.52839	ZNF363
NM_005346.2	0.035714	0.035247	0.10824	-0.5359	HSPA1B
NM_022725.1	0.035714	0.035247	0.023814	-0.53779	FANCF
AI348010	0.035714	0.035247	0.226116	-0.54348	
AI927993	0.035714	0.035247	0.054067	-0.54478	OSBP
BE327172	0.035714	0.035247	0.091317	-0.54925	JUN
AI741876	0.035714	0.00747	0.025182	-0.57505	
NM_003107.1	0.035714	0.035247	0.078087	-0.59709	SOX4
BE383139	0.035714	0.035247	0.00951	-0.60058	RARA
NM_018398.1	0.035714	0.035247	0.016221	-0.603	CACNA2D3
NM_000201.1	0.035714	0.035247	0.036915	-0.62554	ICAM1
NM_002229.1	0.035714	0.035247	0.129802	-0.64436	JUNB
NM_021960.1	0.035714	0.04225	0.024176	-0.66914	MCL1
NM_016010.1	0.035714	0.00747	0.015684	-0.68307	LOC51101
NM_004417.2	0.035714	0.035247	0.043377	-0.68458	DUSP1
NM_025195.1	0.035714	0.035247	0.055882	-0.68638	C8FW
NM_004418.2	0.035714	0.035247	0.306591	-0.68934	DUSP2
AB017493.1	0.035714	0.015406	0.010224	-0.6982	COPEB
AF064824.1	0.035714	0.035247	0.010071	-0.70109	RIPK2
NM_005354.2	0.035714	0.035247	0.04394	-0.70667	JUND
NM_006469.1	0.035714	0.035247	0.006453	-0.71493	NS1-BP
NM_006290.1	0.035714	0.035247	0.155375	-0.73437	TNFAIP3
AI339541	0.035714	0.035247	0.039838	-0.76402	JUND
AF087853.1	0.035714	0.035247	0.076647	-0.77217	GADD45B
AL031602	0.035714	0.035247	0.015158	-0.78504	

BF575213	0.035714	0.035247	0.007144	-0.78651	
M68956.1	0.035714	0.00747	0.001933	-0.79718	MARCKS
NM_004907.1	0.035714	0.035247	0.006503	-0.81053	ETR101
AW083357	0.035714	0.035247	0.009893	-0.81405	IL1RN
AF153820.1	0.035714	0.035247	0.004403	-0.82757	KCNJ2
AI608725	0.035714	0.035247	0.010119	-0.83319	ICAM1
NM_000958.1	0.035714	0.015406	0.003112	-0.86354	PTGER4
AA083483	0.035714	0.035247	0.012228	-0.88452	FTH1
NM_002664.1	0.035714	0.00747	0.000855	-0.88664	PLEK
AL031602	0.035714	0.015406	0.00038	-0.88673	
W27419	0.035714	0.015406	0.000361	-0.95575	
NM_002852.1	0.035714	0.035247	0.001716	-0.97365	PTX3
NM_001964.1	0.035714	0.035247	0.068287	-0.99045	EGR1
AF078077.1	0.035714	0.035247	0.017058	-1.003	GADD45B
NM_015714.1	0.035714	0.035247	0.210858	-1.05996	G0S2
BC004490.1	0.035714	0.035247	0.068201	-1.06388	FOS
AI738896	0.035714	0.035247	0.071526	-1.09453	TNFAIP3
AW973834	0.035714	0.035247	0.030817	-1.09468	
NM_004895.1	0.035714	0.035247	0.004992	-1.10724	CIAS1
U08839.1	0.035714	0.035247	0.030968	-1.1245	PLAUR
BC005020.1	0.035714	0.035247	0.022893	-1.13801	PPIF
NM_005627.1	0.035714	0.035247	0.010834	-1.16132	SGK
NM_015675.1	0.035714	0.035247	0.022251	-1.16822	GADD45B
AI433595	0.035714	0.015406	0.002395	-1.17663	PLEK
NM_002135.1	0.035714	0.035247	0.009942	-1.19934	NR4A1
NM_003407.1	0.035714	0.035247	0.0028	-1.30448	ZFP36
NM_004233.1	0.035714	0.035247	0.045128	-1.33091	CD83
NM_001432.1	0.035714	0.035247	0.001942	-1.33633	EREG
NM_002228.2	0.035714	0.035247	0.007227	-1.34352	JUN
NM_004049.1	0.035714	0.035247	0.004927	-1.41895	BCL2A1
U83981	0.035714	0.035247	0.005806	-1.46885	PPP1R15A
NM_006018.1	0.035714	0.035247	0.002094	-1.50671	HM74
BG491844	0.035714	0.035247	0.011957	-1.61438	JUN
BC002646.1	0.035714	0.035247	0.002438	-1.64136	JUN
NM_000963.1	0.035714	0.035247	0.025772	-1.65759	PTGS2
AY029180.1	0.035714	0.035247	0.011082	-1.69399	PLAUR
NM_014330.2	0.035714	0.035247	0.003245	-1.74665	PPP1R15A
NM_003897.1	0.035714	0.035247	0.002981	-1.89968	IER3
M57731.1	0.035714	0.035247	0.001811	-1.9703	CXCL2
NM_000584.1	0.035714	0.035247	0.030747	-2.54298	IL8
NM_000576.1	0.035714	0.035247	0.000992	-2.66025	IL1B
M15330	0.035714	0.035247	0.001505	-2.71142	IL1B

It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the

invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications, patents, patent applications and sequences identifies by a GenBank accession number mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent, patent application or sequence was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention.

WHAT IS CLAIMED IS:

1. A method of diagnosing a subject with multiple sclerosis, the method comprising determining a level of expression of at least one gene selected from the group consisting of the genes listed in Tables I-V in a sample obtained from the subject, wherein a substantial difference between said level of expression of said gene in said sample obtained from said subject and a normal expression level of said gene is an indication that the subject is afflicted with multiple sclerosis.

2. The method of claim 1, wherein said normal expression level of said at least one gene is determined by measuring said level of expression of said gene in at least one control sample obtained from at least one healthy individual.

3. The method of claim 2, wherein said sample includes peripheral blood mononuclear cells.

4. The method of claim 1, wherein said substantial difference is a difference statistically significant at a confidence level of $p= 0.05$ as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

5. The method of claim 1, wherein said level of expression of said at least one gene is determined by quantifying a level of a protein product thereof in said sample.

6. The method of claim 5, wherein quantifying a level of said protein is effected using a reagent which specifically binds with said protein.

7. The method of claim 6, wherein said reagent comprises an antibody or fragments thereof.

8. The method of claim 1, wherein said at least one gene is selected from the genes listed in Table I.

9. The method of claim 1, wherein said at least one gene is selected from the genes listed in Table II.

10. The method of claim 1, wherein said at least one gene is selected from the genes listed in Table III.

11. The method of claim 1, wherein said at least one gene is selected from the genes listed in Table IV.

12. The method of claim 1, wherein said at least one gene is selected from the genes listed in Table V.

13. The method of claim 1, wherein the level of expression of said at least one gene in said sample is determined by detecting the presence in said sample of a transcribed polynucleotide or portion thereof.

14. The method of claim 13, wherein said transcribed polynucleotide is mRNA.

15. The method of claim 13, wherein said transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with said transcribed polynucleotide or portion thereof.

16. The method of claim 1, wherein said sample from a subject is T cells, and said at least one gene is selected from the genes listed in Table IV and whereas said normal expression of said gene is T-cell expression.

17. The method of claim 16, wherein said substantial difference is at least a 1.5 fold change.

18. The method of claim 1, wherein said at least one gene comprises at least 10 genes each independently selected from the group consisting of the genes listed in Tables I-V.

19. The method of claim 1, wherein said at least one gene comprises at least 50 genes each independently selected from the group consisting of the genes listed in Tables I-V.

20. The method of claim 1, wherein said at least one gene comprises at least 100 genes each independently selected from the group consisting of the genes listed in Tables I-V.

21. The method of claim 1, wherein said at least one gene comprises at least 250 genes each independently selected from the group consisting of the genes listed in Tables I-V.

22. The method of claim 1, wherein said at least one gene comprises at least 500 genes each independently selected from the group consisting of the genes listed in Tables I-V.

23. The method of claim 1, wherein said at least one gene comprises at least 750 genes each independently selected from the group consisting of the genes listed in Tables I-V.

24. The method of claim 1, wherein said at least one gene comprises at least 1000 genes each independently selected from the group consisting of the genes listed in Tables I-V.

25. The method of claim 1, wherein said at least one gene comprises at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V.

26. A method of diagnosing a subject with multiple sclerosis, the method comprising the step of determining a level of expression of each of the genes listed in Tables I-V in a sample obtained from the subject, wherein a substantial difference between expression levels of said genes in said sample obtained from said subject and normal expression levels of said genes is an indication that the subject is afflicted with multiple sclerosis.

27. The method of claim 26, wherein said normal expression levels of said genes is determined by measuring said level of expression of said genes in at least one control sample obtained from at least one healthy individual.

28. The method of claim 29, wherein said sample includes peripheral blood mononuclear cells.

29. The method of claim 26, wherein said substantial difference is a difference statistically significant at a confidence level of $p= 0.05$ as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

30. The method of claim 26, wherein said level of expression of said genes is determined by quantifying a level of a protein product thereof in said sample.

31. The method of claim 30, wherein quantifying a level of said protein is effected using a reagent which specifically binds with said protein.

32. The method of claim 31, wherein said reagent comprises an antibody or fragments thereof.

33. The method of claim 26, wherein the level of expression of said genes in said sample is determined by detecting the presence in said sample of a transcribed polynucleotide or portion thereof.

34. The method of claim 33, wherein said transcribed polynucleotide is mRNA.

35. The method of claim 34, wherein said transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with said transcribed polynucleotide or portion thereof.

36. A method of monitoring a state of multiple sclerosis in a subject, the method comprising monitoring a level of expression of at least one gene selected from the group consisting of the genes listed in Tables I-V over a predetermined time period, wherein substantial difference between the levels of expression of said at least one gene over said predetermined time period indicates a change in a state of the multiple sclerosis in the subject.

37. The method of claim 36, wherein monitoring said level of expression of at least one gene over said predetermined time period is effected

by periodically obtaining a sample from the individual and determining said level of expression of said at least one gene in said sample.

38. The method of claim 37, wherein said sample includes peripheral blood mononuclear cells.

39. The method of claim 36, wherein said substantial difference is a difference statistically significant at a confidence level of p= 0.05 as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

40. The method of claim 36, wherein said level of expression of said at least one gene is determined by quantifying a level of a protein product thereof in said sample.

41. The method of claim 36, wherein quantifying a level of said protein is effected using a reagent which specifically binds with said protein.

42. The method of claim 41, wherein said reagent comprises an antibody or fragments thereof.

43. The method of claim 36, wherein said at least one gene is selected from the genes listed in Table I.

44. The method of claim 36, wherein said at least one gene is selected from the genes listed in Table II.

45. The method of claim 36, wherein said at least one gene is selected from the genes listed in Table III.

46. The method of claim 36, wherein said at least one gene is selected from the genes listed in Table IV.

47. The method of claim 36, wherein said at least one gene is selected from the genes listed in Table V.

48. The method of claim 36, wherein the level of expression of said at least one gene in said sample is determined by detecting the presence in said sample of a transcribed polynucleotide or portion thereof.

49. The method of claim 48, wherein said transcribed polynucleotide is mRNA.

50. The method of claim 48, wherein said transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with said transcribed polynucleotide or portion thereof.

51. The method of claim 36, wherein said sample from a subject is T cells, and said at least one gene is selected from the genes listed in Table IV and whereas said normal expression of said gene is T-cell expression.

52. The method of claim 51, wherein said substantial difference is at least a 1.5 fold change.

53. The method of claim 36, wherein said at least one gene comprises at least 10 genes each independently selected from the group consisting of the genes listed in Tables I-V.

54. The method of claim 36, wherein said at least one gene comprises at least 50 genes each independently selected from the group consisting of the genes listed in Tables I-V.

55. The method of claim 36, wherein said at least one gene comprises at least 100 genes each independently selected from the group consisting of the genes listed in Tables I-V.

56. The method of claim 36, wherein said at least one gene comprises at least 250 genes each independently selected from the group consisting of the genes listed in Tables I-V.

57. The method of claim 36, wherein said at least one gene comprises at least 500 genes each independently selected from the group consisting of the genes listed in Tables I-V.

58. The method of claim 36, wherein said at least one gene comprises at least 750 genes each independently selected from the group consisting of the genes listed in Tables I-V.

59. The method of claim 36, wherein said at least one gene comprises at least 1000 genes each independently selected from the group consisting of the genes listed in Tables I-V.

60. The method of claim 36, wherein said at least one gene comprises at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V.

61. A method of assessing the efficacy of a treatment regimen on multiple sclerosis in a subject, the method comprising determining a level of

expression of at least one gene selected from the group consisting of the genes listed in Tables I-V in samples obtained from the subject prior to, and following exposure to the treatment regimen, wherein a substantial difference in the expression level of said at least one gene between said samples is an indication that the treatment regimen is efficacious in treating multiple sclerosis in said subject.

62. The method of claim 61, wherein said treatment regimen is administering at least one test compound for inhibiting multiple sclerosis.

63. The method of claim 61, wherein said treatment regimen is an environmental condition.

64. The method of claim 61, wherein said samples include peripheral blood mononuclear cells.

65. The method of claim 61, wherein said substantial difference is a difference statistically significant at a confidence level of $p= 0.05$ as determined by at least one test selected from the group consisting of a t-test, a TNoM and an INFO score.

66. The method of claim 61, wherein said level of expression of said at least one gene is determined by quantifying a level of a protein product thereof in said sample.

67. The method of claim 66, wherein quantifying a level of said protein is effected using a reagent which specifically binds with said protein.

68. The method of claim 67, wherein said reagent comprises an antibody or fragments thereof.

69. The method of claim 61, wherein said at least one gene is selected from the genes listed in Table I.

70. The method of claim 61, wherein said at least one gene is selected from the genes listed in Table II.

71. The method of claim 61, wherein said at least one gene is selected from the genes listed in Table III.

72. The method of claim 61, wherein said at least one gene is selected from the genes listed in Table IV.

73. The method of claim 61, wherein said at least one gene is selected from the genes listed in Table V.

74. The method of claim 61, wherein the level of expression of said at least one gene in said samples is determined by detecting the presence in said samples of a transcribed polynucleotide or portion thereof.

75. The method of claim 74, wherein said transcribed polynucleotide is mRNA.

76. The method of claim 74, wherein said transcribed polynucleotide or portion thereof is detected via a labeled probe which specifically hybridizes with said transcribed polynucleotide or portion thereof.

77. The method of claim 61, wherein said at least one gene comprises at least 10 genes each independently selected from the group consisting of the genes listed in Tables I-V.

78. The method of claim 61, wherein said at least one gene comprises at least 50 genes each independently selected from the group consisting of the genes listed in Tables I-V.

79. The method of claim 61, wherein said at least one gene comprises at least 100 genes each independently selected from the group consisting of the genes listed in Tables I-V.

80. The method of claim 61, wherein said at least one gene comprises at least 250 genes each independently selected from the group consisting of the genes listed in Tables I-V.

81. The method of claim 61, wherein said at least one gene comprises at least 500 genes each independently selected from the group consisting of the genes listed in Tables I-V.

82. The method of claim 61, wherein said at least one gene comprises at least 750 genes each independently selected from the group consisting of the genes listed in Tables I-V.

83. The method of claim 61, wherein said at least one gene comprises at least 1000 genes each independently selected from the group consisting of the genes listed in Tables I-V.

84. The method of claim 61, wherein said at least one gene comprises at least 1200 genes each independently selected from the group consisting of the genes listed in Tables I-V.

85. A kit for diagnosing multiple sclerosis in a subject, the kit comprising components suitable for determining expression levels of at least one gene selected from the group of genes listed in Tables I-V.

86. The kit of claim 85, wherein said reagents include at least one polynucleotide sequence selected capable of specifically hybridizing with an transcription product of said at least one gene and reagents for detecting and optionally quantifying a complex formed from said at least one polynucleotide sequence and said transcription product.

87. The kit of claim 85, wherein said reagents include at least one antibody selected capable of specifically binding a polypeptide product of said at least one gene and reagents for detecting and optionally quantifying a complex formed from said at least one antibody and said polypeptide product.

88. The kit of claim 85, wherein said at least one gene is selected from the genes listed in Table I.

89. The kit of claim 85, wherein said at least one gene is selected from the genes listed in Table II.

90. The kit of claim 85, wherein said at least one gene is selected from the genes listed in Table III.

91. The method of claim 88, wherein said at least one gene is selected from the genes listed in Table IV.

92. The method of claim 85, wherein said at least one gene is selected from the genes listed in Table V.

93. The kit of claim 85, wherein the kit further comprises packaging material identifying the kit as useful from diagnosing MS.

94. A polynucleotide array comprising at least 10 and no more than 1500 polynucleotide sequences, wherein each of said sequences is selected capable of hybridizing with a transcription product of a polynucleotide sequence of a gene selected from the group of genes listed in Tables I-V.

95. The polynucleotide array of claim 94, wherein said array is selected having polynucleotide sequences capable of diagnosing subjects suspected of suffering from multiple sclerosis.

96. The polynucleotide array of claim 94, wherein said array is selected having polynucleotide sequences capable of diagnosing subjects suspected of suffering from probable multiple sclerosis.

97. The polynucleotide array of claim 94, wherein said array is selected capable of diagnosing subjects suspected of suffering from primary progressive multiple sclerosis.

98. The polynucleotide array of claim 94, wherein said array is selected capable of diagnosing subjects suspected of suffering from relapsing multiple sclerosis.

99. The polynucleotide array of claim 94, wherein said gene is selected from the genes listed in Table I.

100. The polynucleotide array of claim 94, wherein said gene is selected from the genes listed in Table II.

101. The polynucleotide array of claim 94, wherein said gene is selected from the genes listed in Table III.

102. The polynucleotide array of claim 94, wherein said gene is selected from the genes listed in Table IV.

103. The polynucleotide array of claim 94, wherein said gene is selected from the genes listed in Table V.

104. An array comprising at least 10 and no more than 1500 antibodies or antibody fragments each capable of specifically binding a protein product of a gene selected from the group of genes listed in Tables I-V.

105. The array of claim 104, wherein said array is selected having antibodies or antibody fragments capable of diagnosing subjects suspected of suffering from multiple sclerosis.

106. The array of claim 104, wherein said array is selected having antibodies or antibody fragments capable of diagnosing subjects suspected of suffering from probable multiple sclerosis.

107. The array of claim 104, wherein said array is selected capable of diagnosing subjects suspected of suffering from primary progressive multiple sclerosis.

108. The array of claim 104, wherein said array is selected capable of diagnosing subjects suspected of suffering from relapsing multiple sclerosis.

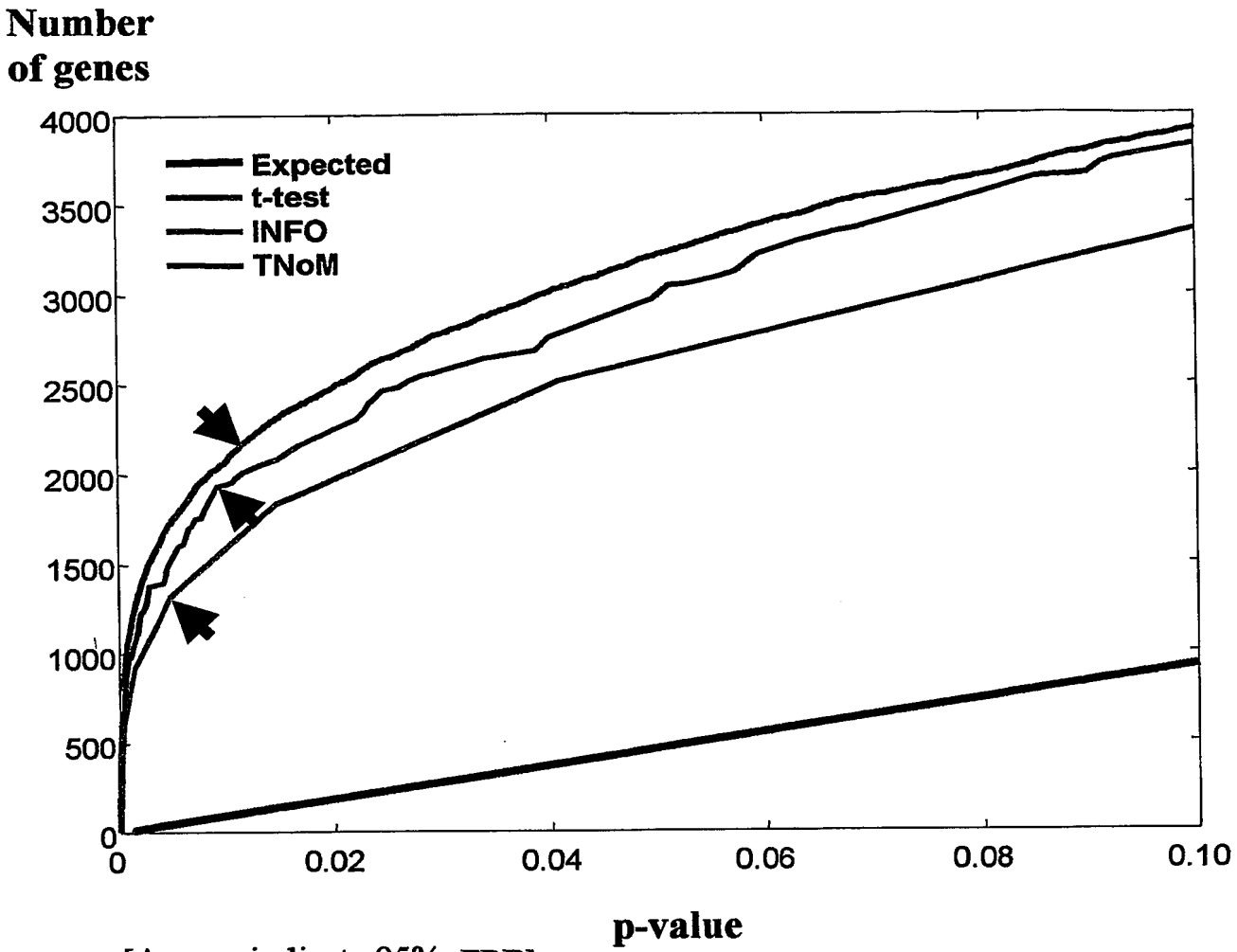
109. The array of claim 104, wherein said gene is selected from the genes listed in Table I.

110. The array of claim 104, wherein said gene is selected from the genes listed in Table II.

111. The array of claim 104, wherein said gene is selected from the genes listed in Table III.

112. The array of claim 104, wherein said gene is selected from the genes listed in Table IV.

113. The array of claim 104, wherein said gene is selected from the genes listed in Table V.



[Arrows indicate 95% FDR]

FIGURE 1A

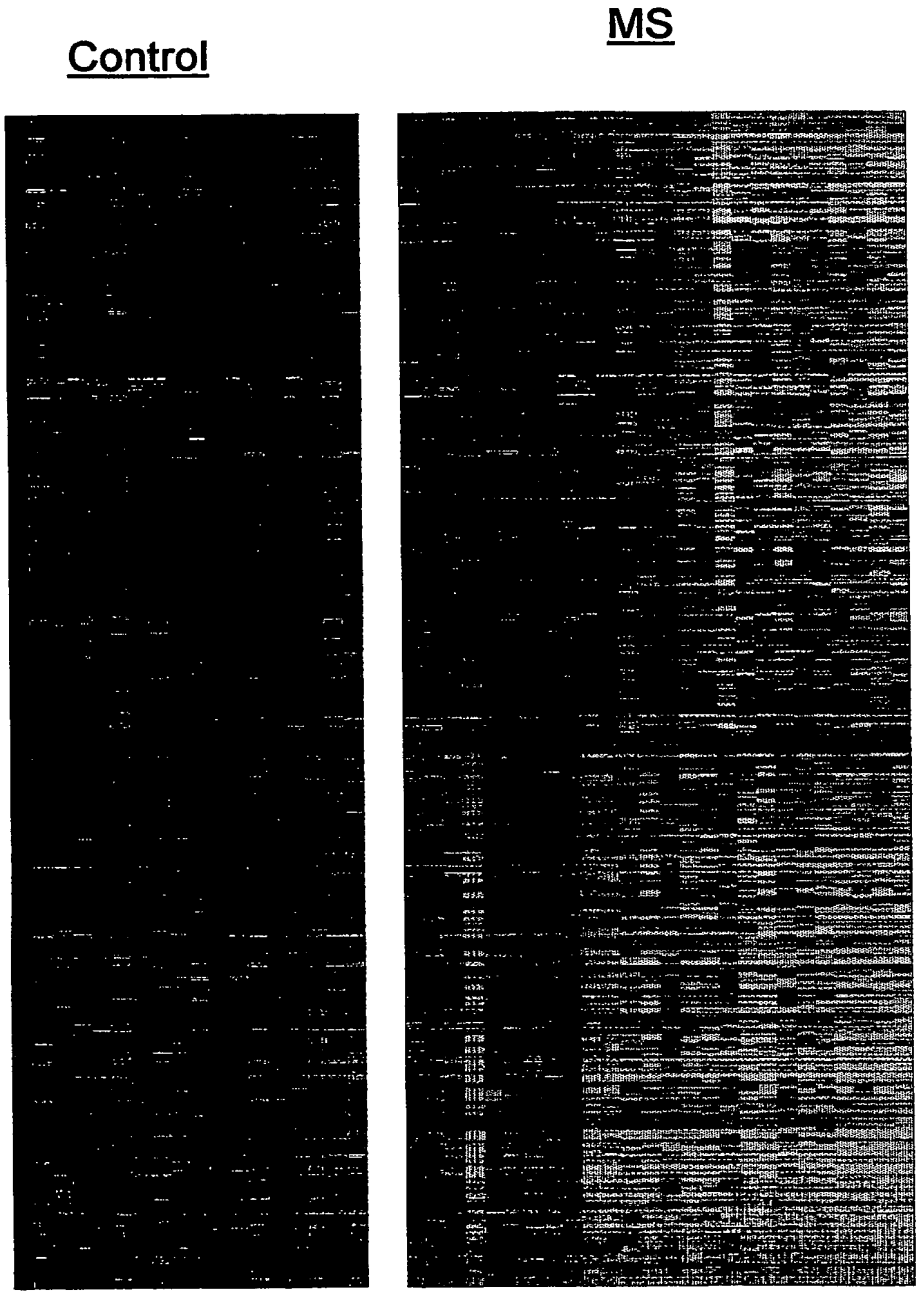


FIGURE 1B

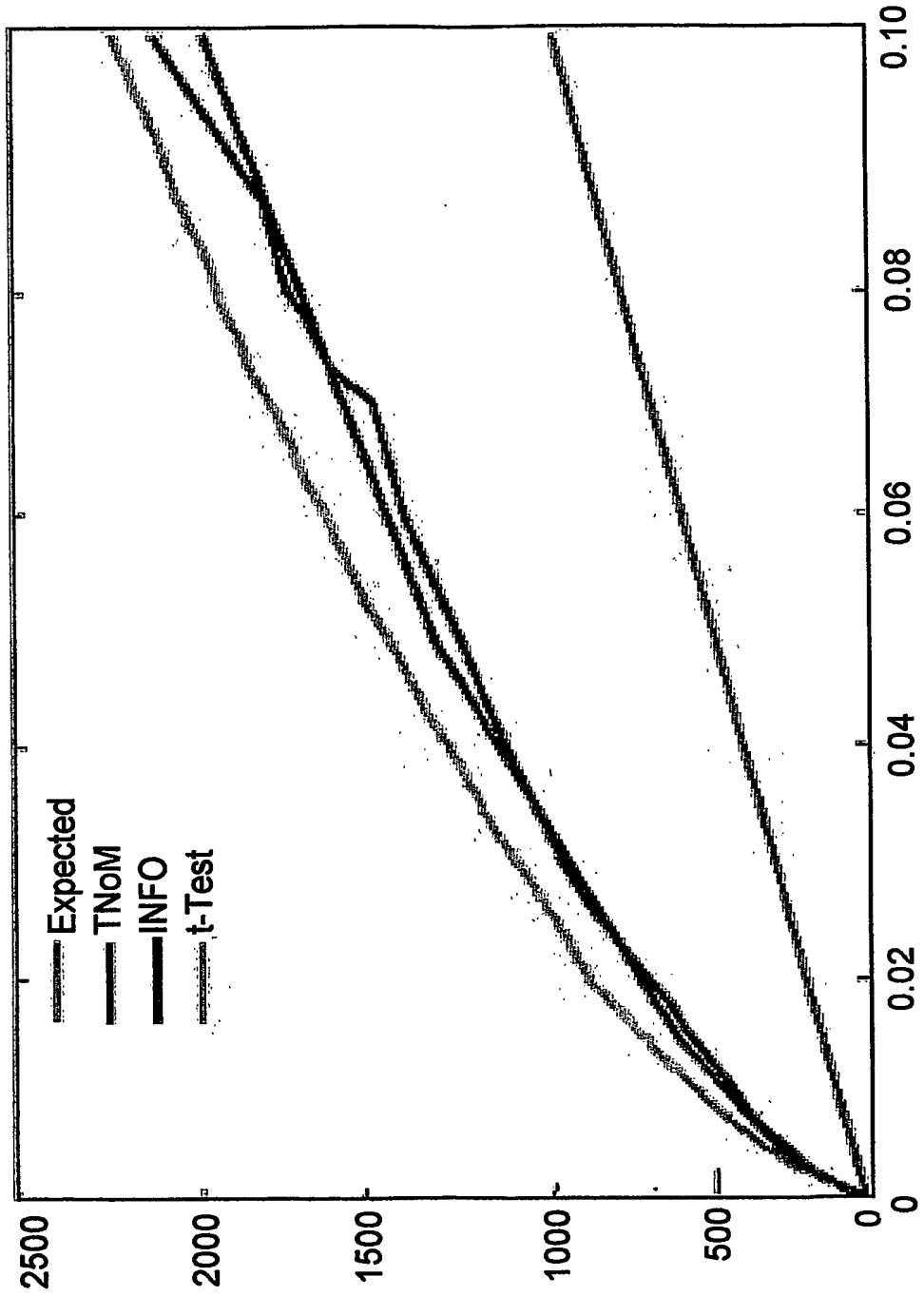

Expected
TNoM
INFO
t-Test
2500
2000
1500
1000
500
0
0
0.02
0.04
0.06
0.08
0.10

FIGURE 2A

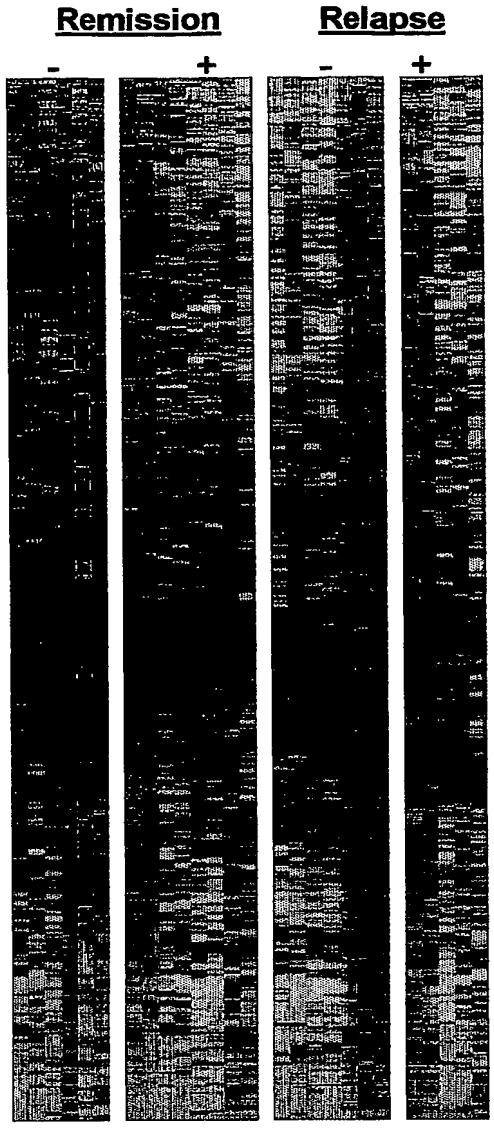


FIGURE 2B

FIGURE 3

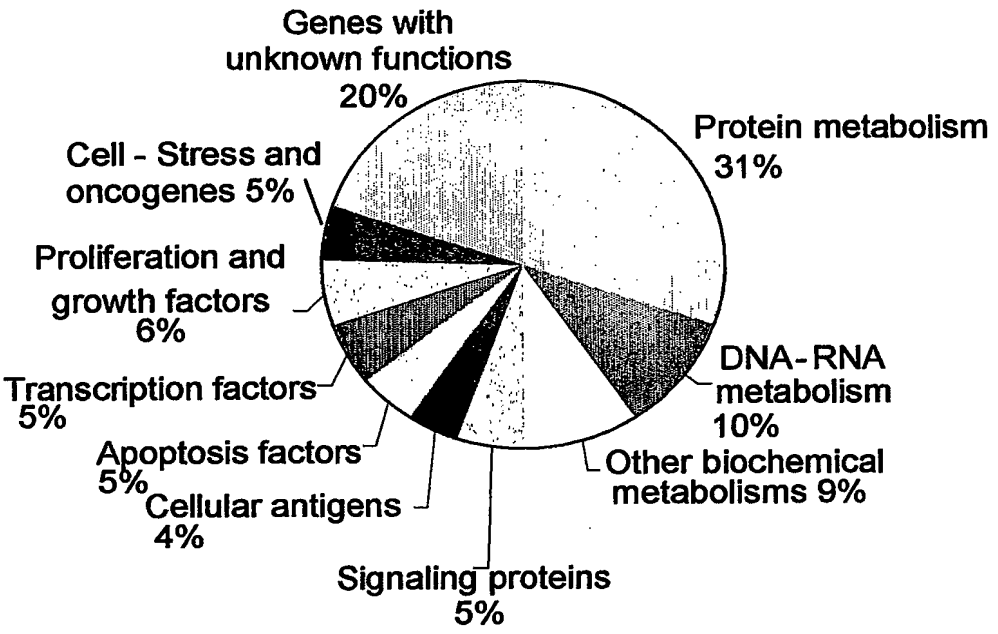
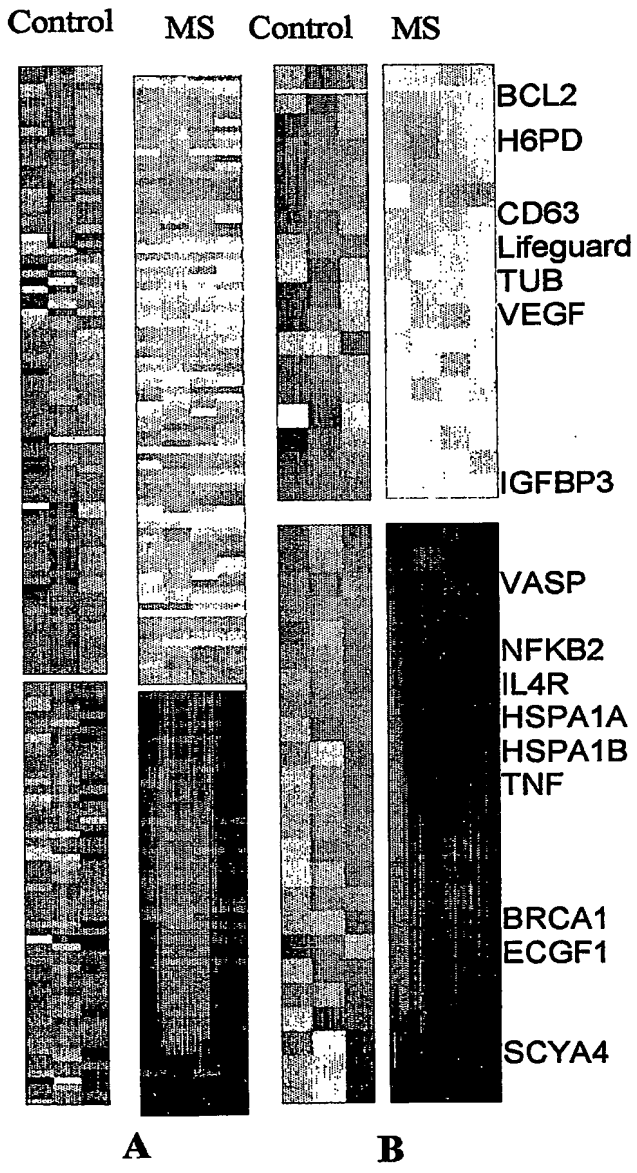

Genes with unknown functions 20%
Protein metabolism 31%
Cell - Stress and oncogenes 5%
Proliferation and growth factors 6%
Transcription factors 5%
DNA-RNA metabolism 10%
Apoptosis factors 5%
Other biochemical metabolisms 9%
Cellular antigens 4%
Signaling proteins 5%

FIGURE 4


Control
MS
Control
MS
BCL2
H6PD
CD63
Lifeguard
TUB
VEGF
IGFBP3
VASP
NFKB2
IL4R
HSPA1A
HSPA1B
TNF
BRCA1
ECGF1
SCYA4
A
B

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(81) Designated States *(national)*: AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK (utility model), SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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17 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2003/081201 A3

(54) Title: PERIPHERAL BLOOD CELL MARKERS USEFUL FOR DIAGNOSING MULTIPLE SCLEROSIS AND METHODS AND KITS UTILIZING SAME

(57) Abstract: Markers of multiple sclerosis and methods and kits utilizing same for diagnosing multiple sclerosis in an individual are provided.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL03/00208

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; C07H 21/04
US CL : 435/6,91.2; 536/23.1, 24.3
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6,91.2; 536/23.1, 24.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	" Genes, environment, and susceptibility to multiple sclerosis", Neurobiology of Disease, 17(2004)pp 131-143	1-35
A	"Are we there yet?": Deciding when one has demonstrated specific genetic causation in complex diseases and quantitative traits", Am. J. Hum. Genet. 73:711-719, 2003	1-35
Y	US 6,132,977 (Thompson et al.) 17 Oct 2000 (17.10.2000), column 3 and 5	1-35
Y	"In vivo gene expression revealed by cDNA arrays: the pattern in relapsing-remitting multiple sclerosis patients compared with normal subjects", J. of Neuroimmunology, 116 (2001) p. 213-219	1-35
Y	"Regulated Secretion in Platelets: Identification of Elements of the Platelet Exocytosis Machinery", Blood, vol. 90, no. 4 (Aug 15) 1997: pp 1490-1500	1-35
A	"Distributation of Soluble N-ethylmaleimide Fusion Protein attachment Proteins (SNAPs) in the Rat Nervous System", Neuroscience, vol. 107, no. 3, pp. 363-71 (2001)	1-35
Y	"Soluble NSF-attachment proteins", The International Journal of Biochemistry and Cell Biology, 30 (1998) 573-77	1-35

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
07 January 2005 (07.01.2005)

Date of mailing of the international search report
02 FEB 2005

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Authorized officer
Sarae Bausch
Telephone No. (571)272-0500

Form PCT/ISA/210 (second sheet) (July 1998)

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claim(s) 1-35, drawn to a method of diagnosing a subject with multiple sclerosis by differential gene expression of a gene listed in tables I-V.

Group II, claims 36-60, a method for monitoring the state of multiple sclerosis by differential gene expression of a gene listed in tables I-V.

Group III, claims 61-85, a method of assessing the efficacy of treatment of multiple sclerosis by differential gene expression of a gene listed in tables I-V.

Group IV, claims 86-93, a kit containing components for determining expression level of a gene from tables I-V.

Group V, claims 94-103, a polynucleotide array capable of hybridizing a transcription product of a gene from tables I-V.

Group VI, claims 104-113, an antibody array capable of binding a protein product from the group of genes in tables I-V.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Each group contains multiple species of invention where each species is a particular combination of sequences examined from the tables in the specification. For example, each group of " one" is a separate species, each group of "two" is a separate species and so forth. There are millions of possible combinations available for search.

The first named invention, Group I, claims 1-35 with respect to the first named gene NAPG will be searched.

For each additional combination applicant desires to be searched within a claim set. Applicant must indentify the combination and pay an additional $210 for the search of a particular method or product that includes the particular combination of genes.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature that joins all of these inventions is that they are utilized or are differentially expressed genes in multiple sclerosis. It was known at the time of the invention that differentially expressed genes exist in multiple sclerosis patients versus healthy patients (see Whitney et al, Annals of Neurology, 1999, v46, p425-8) and thus is not a special technical feature in view of the PCT Rules. Group I is the first named invention including methods for diagnosing multiple sclerosis. Group 4 includes the first named product for determining expression level of genes, comprising gene NAPG, GenBank U78107 from Table I, which is known. There is no special technical feature that joins the first named method and the first named product as the gene of group 4 is anticipated over the prior art, see GenBank accession. The remaining groups include additional products and methods that are not linked by a unifying inventive concept as they are drawn to unique product and methods and are so separately grouped.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each is drawn to a unique nucleic acid sequence or polymorphism that does not share a common structure with the others.

Furthermore, considering all of the possible groupings of genes, there are a multiplicity of groups (i.e. species) and the number of which is effectively unable to be calculated. If applicant wishes for additional genes or combinations of genes to be searched, a fee must be paid for each additional combination. If applicant wished to pay for additional inventions, applicant must identify the specific gene or combinations by their location within the tables and will be required to pay an additional $210 per gene or gene combination selected.

Continuation of B. FIELDS SEARCHED Item 3:
East, Medline, STN (medline, cancerlit, biosis, caplus)
search terms: multiple sclerosis and gene expression, multiple sclerosis and SNAP, SNAP, gamma-SNAP

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL03/00208

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-35 and first named gene NAPG

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

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